BRAIN.

PART 1, VOL. 50.

ENCEPHALITIS PERIAXIALIS DIFFUSA. REPORT OF THREE CASES WITH PATHOLOGICAL EXAMINATIONS.

BY T. GRAINGER STEWART, M.D., F.R.C.P.,
Physician to the National Hospital, Queen Square;

J. GODWIN GREENFIELD, M.D., F.R.C.P.,
Pathologist to the National Hospital;

AND

MARJORIE A. BLANDY, M.B., M.R.C.P.,
Assistant Physician to the Elizabeth Garrett Anderson Hospital, late Registrar to the National Hospital, Queen Square.

WHEN Schilder in 1912 [10] named a certain type of sclerosis of the brain "encephalitis periaxialis diffusa" he grouped under this heading a number of cases characterized by diffuse demyelination of the centrum ovale, which was more or less symmetrical in the two hemispheres, and which, at least in the majority of cases, affected the occipital lobes at an early stage. Records of subsequent cases have confirmed this general conception of the disease, but, as is usual, at the same time have amplified it, and made the distinction of this from other types of brain sclerosis a little indefinite. In particular, certain cases have been reported as Schilder's encephalitis which approximate very closely to the classical pathological picture of disseminated sclerosis, and at least one case of Schilder's encephalitis has been classified as "disseminated sclerosis in childhood." This confusion is increased by the similarity of the lesions in these two diseases, particularly when they occur in the brain-stem, and also by our complete ignorance of the ætiology of either disease.

The three cases we report here belong undoubtedly to the type which Schilder described, but they differ from one another in many ways, both in the clinical picture and in the pathological appearances.

In addition they present several features which either have not been previously described, or on which too little emphasis has been laid.

On the clinical side two important facts appear. First, that the disease may kill with great rapidity, even in such a short period as nine days. Secondly, that the first symptom may be deafness of central origin, which may precede other symptoms, such as blindness, by some months.

On the pathological side the most important observation is that the disease is not either necessarily, nor even perhaps usually, confined to the centrum ovale of the cerebral hemispheres, but may affect other parts of the central nervous system such as the pons, the optic nerves and the cervical cord.

Our cases thus serve to enlarge our knowledge of the disease in its somewhat protean manifestations, and to furnish further criteria for its differential diagnosis.

Case 1.—W. W., male, aged 8, was admitted into St. James's Hospital, Balham, on May 17, 1922. While in hospital he was seen by Dr. Grainger Stewart, and we are indebted to Dr. Piggott, under whose immediate care he was, for the following notes on his history and condition. The history obtained from his mother was that eighteen months before admission he had had eleven teeth extracted, and since that time he had not been as well as before. Eight months before admission he was seen by the school medical officer who noted that he was dull and listless and rather deaf. This deafness increased steadily. Five months before admission his sight began to fail and he became weak in the legs. He did not complain of headache and his habits remained clean.

On admission in May, 1922, the patient, a thin pale child, was found to be blind and totally deaf, but able to walk a little. The reflexes were normal. No record was kept of the ophthalmoscopic examination. The Wassermann reaction of the blood and cerebro-spinal fluid was negative.

After a week in hospital he was taken home by his parents, who however brought him back a month later as his condition had become very much worse. He was quite helpless and was completely incontinent but was able to swallow. He was absolutely blind and there was no sign of response when light was thrown on to his eyes. His pupils were large and did not respond to light.

Ophthalmoscopic examination showed both discs to be atrophic, of a papery white colour and without any evidence of previous neuritis. The position of the eyes was inconstant and nystagmus of varying type was noted at different times. His deafness was complete. He had a left-sided hemiplegia, but both plantar reflexes were extensor in type. The deep reflexes were increased. A provisional diagnosis of tumour of the pons was made. He died on August 7, 1922, after an illness of at least eleven, and probably of twenty months' duration.

A complete post-mortem examination was made, without however the discovery of any disease apart from that in the brain. This was cut across in

horizontal section, and after hardening in formalin solution the cerebral hemispheres were brought to the laboratory of the National Hospital where a histological examination was made of them. It is unfortunate in view of our findings in the other two cases that no examination of the brain-stem and cerebellum was made.

On naked-eye examination of horizontal sections it was noted that the white matter of the occipital and temporal lobes was greyish and very tough. The area of white matter involved was roughly symmetrical, and extended into the visual cortex where it closely surrounded the grey matter of the calcarine fissure, but spared a thin zone of myelinated fibres under the cortex. It passed however into the fine ramifications of white matter of the occipital cortex. Towards the external surface of the occipital lobe a wider zone of white matter was left intact, but in the temporal poles the sclerosis extended right up to the subcortical arcuate fibres. The sclerosis was confined to the lower and posterior parts of the brain; it did not pass forwards beyond

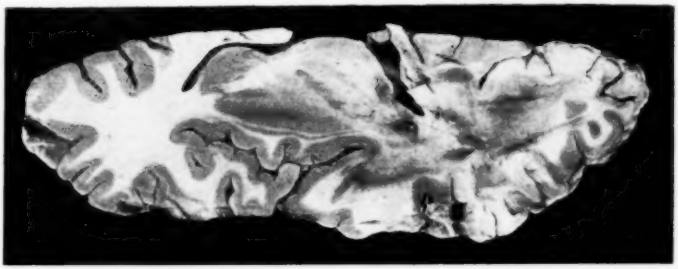


FIG. 1 (*Case* 1).—Section of brain through basal ganglia showing gelatinous degenerated area in occipital pole.

the hindmost end of the internal capsule, nor upwards above the level of a horizontal section passing through the upper part of the body of the caudate nucleus (fig. 1).

Microscopically this sclerosed area was found to be completely demyelinated except for a few broken and beaded myelin sheaths which could be seen sparsely scattered throughout it (fig. 2). By Bielschowsky's staining method a rather larger number of irregularly contorted axis-cylinders could be seen in it, but these also had for the most part disappeared. The degenerated axons were replaced by a dense feltwork of neuroglia in which were many large cell bodies. Of these the majority were multinucleated, usually with a zone of nuclei round the periphery. In some the protoplasm was continued into a leash of fine processes which passed from one or two poles of the cell, but others appeared to be completely devoid of processes. The latter form corresponded exactly to the "globoid cells" described by Collier and Greenfield [4] in the second case reported by them.

Cells of this special form were only seen in regions where the sclerosis seemed to be of comparatively recent date. They were not found in the more central parts of the occipital lobes. In sections stained by Scharlach R. it was noticeable that although numerous typical compound granular corpuscles could be seen, the neuroglial cells did not contain fat. Where fatty globules were abundant, as in the more recently diseased areas, they were often collected in a thin zone around neuroglial cells, but did not appear to pass into their cytoplasm. In such regions there was a considerable degree of perivascular infiltration, partly with compound granular corpuscles, and partly with small lymphocyte-like cells. There was also a definite fibrous thickening of the adventitial and peri-adventitial coats of the small vessels. In other regions,

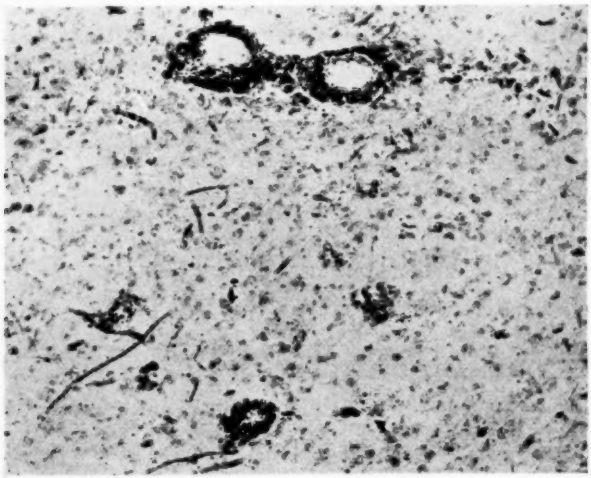


FIG. 2 (*Case* 1).—Section of degenerated area stained by Weigert-Pal and carmine; showing a few broken myelin sheaths and numerous droplets of myelin collected in fat granule cells around the blood-vessels.

where the sclerosis appeared to be of older standing, there was very little accumulation of fatty droplets and little or no perivascular infiltration. In these regions all the neuroglial cells were of the spider-cell type and the feltwork of neuroglial fibres was particularly dense.

Passing from the diseased tissue to more normal areas of white matter, there was still to be seen a general diffuse neuroglial overgrowth, with a few enlarged neuroglial cells and some scattered compound granular corpuscles. There was no general excess of neuroglial nuclei, but rather a slight enlargement of the cytoplasm and increase in number and thickness of their fibres. In addition the cytoplasm of many of the interfascicular glial cells was swollen, and mucin granules could be demonstrated in many of these cells when stained by mucicarmine.

In the cortex comparatively slight changes could be seen. The sub-pial zone of neuroglia was rather denser than normal, and numerous astrocytes were present in the deepest cortical layers. A few compound granular corpuscles were present in the perivascular sheaths of some of the fine vessels which penetrated the cortex. The nerve-cells and fibres of the cortex, as seen by neurofibril and myelin stains, appeared well preserved. The arcuate fibres stained rather palely, and appeared as a zone of very fine fibres; by Scharlach R. staining this zone was found to contain very many compound granular corpuscles. The transition, therefore, from normal to pathological on leaving the cortex and approaching the white matter was very abrupt, very much more so indeed than the transition from normal white matter to an area of sclerosis.

We shall need to refer to this fact when considering the distinction between this disease and disseminated sclerosis.

Summary of Case 1.—Boy, aged 8. History first of deafness and mental apathy, then of blindness, hemiplegia and finally complete helplessness, the illness lasting about twelve to eighteen months.

Brain lesion.—A diffuse sclerosis of the white matter of the occipital and temporal lobes, leaving the cortex and the subcortical white matter intact. This sclerosis is characterized by almost complete destruction of myelin sheaths and to a slightly less degree of axis cylinders, and by the replacement of these by a dense neuroglial overgrowth. Numerous compound granular corpuscles and perivascular collections of mononuclear cells are found in the more recently diseased areas.

Case 2.—R. M., female, aged 3. This child was admitted to the Hospital for Sick Children, Great Ormond Street, on January 8, 1923, under the care of Dr. F. J. Poynton, to whom we are indebted for the clinical records and for permission to publish the case. The history was that for three weeks she had had a cough and a cold in the head. One week before admission attacks of gasping had occurred throughout the day, and since then she had vomited about once each day. She had slept poorly and had called out in her sleep. She had been constipated, and she had become more irritable than usual. What was described as a "convulsion" had occurred on the day of admission.

There was nothing of importance in the family history, and she had had no previous illnesses.

On examination she was well nourished, but her eyes were sunken and the facial expression vacant. The limbs were cold and blue, the skin dry and inelastic. A squint was noticed on the day of admission, but was absent on subsequent examination. There was no other cranial nerve palsy. The pupils reacted well, and there was no optic nystagmus. The knee-jerks were present, the abdominal reflexes absent. The right plantar reflex gave a normal response, the left a doubtful Babinski sign. Kernig and Brudzinski signs were absent.

Ophthalmoscopic examination of the left eye showed a clearly defined disc. No record of the appearance of the right fundus was kept. A lumbar puncture was performed, and clear colourless cerebro-spinal fluid was obtained which did not form any coagulum. It contained ten to fifteen lymphocytes per cubic millimetre, 60 mg. of protein and 760 mg. of chlorides per 100 c.c. Glucose was present in approximately normal quantity. Cultures of the fluid remained sterile.

For the first few days after admission the child was very drowsy, but could be roused. When not asleep, she had a somewhat vacant stare. She cried out at times, occasionally vomited and sometimes drew up her legs and screamed. The plantar reflexes were sometimes of the Babinski type. There was no rigidity of the neck muscles.

Towards the end of January she improved mentally and could understand and do what she was told. On February 12 it was noted that she could sit up; she answered questions and smiled somewhat fatuously when spoken to. Soon after this she was taken home.

She was re-admitted on April 10 of the same year. In the interval she had developed a high-stepping gait and tremor of the hands and arms. On the night before admission she had fallen off a chair on to her head.

On examination on April 10 she was found to be unable to sit up without support, but she appeared to understand what was said to her. The movements of the limbs were unimpaired. There was a curious trembling movement of the jaw when she cried. On the following day she was drowsy. The pupils were unequal and all the tendon jerks were exaggerated. The plantar reflexes were both of the Babinski type. The fundus oculi was normal on each side and there was no sign of blindness. The Wassermann reaction of the blood was examined and found to be normal. The cerebro-spinal fluid was examined for urea and 156 mg. per 100 c.c. were found.

She became completely unconscious on April 13th and died on the 15th.

A post-mortem examination was performed on the following day. No abnormality was found on external examination of the brain and spinal cord except that they appeared somewhat congested. No hydrocephalus or obvious hæmorrhage was seen. The brain was brought to the laboratory of the National Hospital for further examination, and horizontal sections across the hemisphere revealed large areas of granular softening of the centrum ovale, an appearance from which the diagnosis of Schilder's form of encephalitis could be made at once. The distribution of these areas was somewhat different from that in Case 1, although in this case also they affected the white matter of the occipital lobes more than that of the frontal lobes. But whereas in Case 1 they were confined to the lower parts of the brain, in this case they were most pronounced in the upper regions of white matter and even invaded the white centres of the vertical convolutions. With the exception of small areas of softening on the outer aspect of the posterior horns of the lateral ventricles, there was no evidence of disease below a horizontal section passing immediately under the genu and splenium of the corpus callosum (*coup d'élection*). The

basal ganglia were normal to naked-eye examination, and no evidence of disease in the cerebellum or brain-stem could be seen. After fixation the areas of softening were brownish in colour, and on section gave a rough granular surface. They were most intense around the lateral ventricles, especially the posterior horn, where they formed almost symmetrical fan-shaped areas extending into the convolutions of the occipital poles, but at a rather higher level than the visual cortex. The consistence of the brain tissue in these areas may be judged from the fact that although slabs 5 mm. thick remained entire it was practically impossible to cut frozen sections which would hold together, even at 30μ. There was, however, no vacuolation or gross loss of brain substance (figs. 3A and 3B).

Microscopically these areas were characterized by a diffuse demyelination, similar to that found in Case 1, but less complete and sparing the axis-cylinders to a greater extent. Neuroglial overgrowth was very slight; there was throughout the affected regions a great increase in the number of neuroglial nuclei, but no overgrowth of fibres could be made out by the Victoria blue stain used to demonstrate them. In sections stained with Scharlach R. the tissues appeared thinned out, with numerous small vacuoles which may have been largely due to shrinkage in the reagents employed. Almost all the myelin sheaths were disintegrated and the myelin collected into red-staining masses in which it had lost its power of double refraction. Some of these collections were in compound granular corpuscles, but others were free in the tissues. A few cholesterin crystals, which remained unstained with Scharlach R., were the only doubly refractile elements seen. Those few myelin sheaths that were left were contorted, beaded or swollen into fairly large balls.

Sections of less severely affected areas were stained with alum hæmatoxylin and muci-carmine. This stain demonstrated very numerous small granules of mucin, irregularly rounded and rather larger than the nuclei of the interfascicular glial cells, which were greatly multiplied. In addition some larger hyaline bodies could be seen here and there which did not stain by muci-carmine. No perivascular infiltration was present anywhere in any of the sections examined, and there were comparatively few typical compound granular corpuscles. There was also a complete absence of enlarged or multinucleated neuroglial astrocytes or of spider cells.

Frozen sections of the brain-stem and cerebellum stained by Scharlach R. gave evidence of disease in the pons which was not seen on naked-eye examination. This consisted of areas of myelin destruction in the upper half of the pons, among the fibres of the pyramidal tract and in the corpus trapezoides. Here the myelin sheaths were beaded or more or less completely demyelinated, and very numerous compound granular corpuscles were seen scattered irregularly and grouped around the small vessels. Similar sections stained by the Weigert-Pal method presented comparatively little alteration except that the affected regions were paler than normal. There was not the sharply defined distinction between normal and demyelinated areas which we shall describe in the pons in Case 3. There was, in addition, evidence of slight

degeneration of the pyramidal tracts both in the mid-brain and medulla, in that a few vessels in this region were ringed with compound granular corpuscles. The pyramidal tracts did not, however, show any gross demyelination, and in Weigert-Pal sections appeared to be well stained. In the cerebellum also there was a slight accumulation of lipoid in the endothelial cells of the small vessels both in the molecular layer and within and just internal to the granular layer. There was no evidence of degeneration of the white matter of the cerebellum or of the Purkinje cells, and cells of the nucleus dentatus appeared normal.

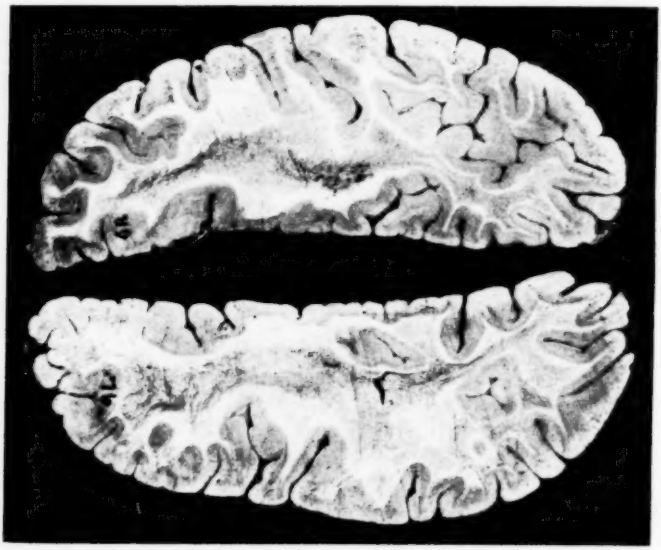


FIG. 3A (*Case* 2).—Slabs of brain showing the distribution of the lesions.

Summary of Case 2.—A girl, aged 3, became rapidly ill with cerebral symptoms, attacks of gasping, vomiting and irritability followed by drowsiness. The abdominal reflexes were lost and there was an unilateral and at times a bilateral Babinski sign. There was no evidence of meningitis. Slight excess of cells and protein were found in the cerebro-spinal fluid. Temporary improvement occurred after about a month of illness, so that she could sit up, walk with help and answer questions intelligently, but during this remission she developed high-stepping gait, and tremor of the hands, arms and jaw. About three months after the onset of the illness she became rapidly comatose and

died. The total duration of the illness was three and a half months. She had shown no evidence of blindness, and ophthalmoscopic examination revealed no disease of the fundi.

On post-mortem examination symmetrical brown granular areas of softening were found in the white matter of the parietal and occipital lobes of the cerebrum, especially towards the upper part of the parietal lobes. There were also isolated patches of partial demyelination in the

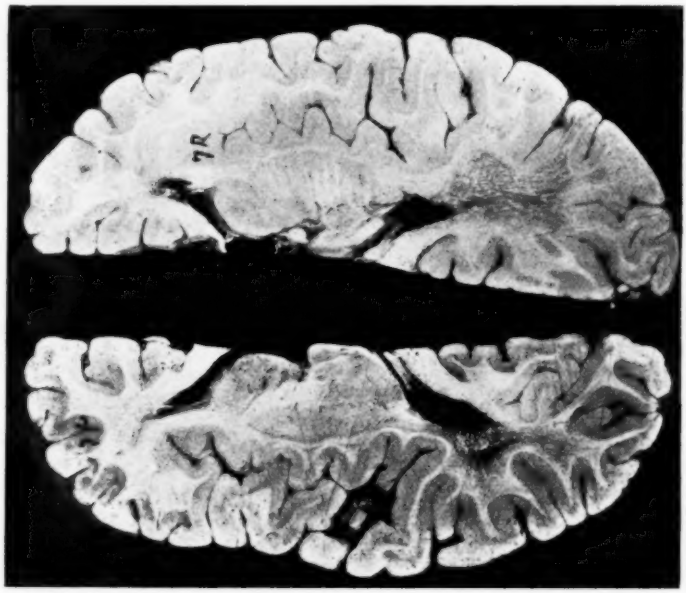


FIG. 3B (*Case* 2).—Slabs of brain showing the distribution of the lesions.

pons. Microscopically these areas were found to be severely demyelinated and to show in addition a partial destruction of axis-cylinders. Except for some proliferation of neuroglial nuclei and for the formation of mucin droplets in and between the bodies of the interfascicular glial cells, there was no neuroglial reaction. Compound granular corpuscles were scanty and there was no perivascular infiltration.

Case 3.—D. W., a widow, aged 43.

Previous health good except for attacks of "bilious headache" (migraine) from which she had suffered for years. These attacks occurred every two to three months.

Present illness.—On the morning of June 10, 1925, she felt in her ordinary health and went to her charring work as usual. At 5 p.m. she stopped work as the sight of the right eye had suddenly become dim. She went home but did not feel ill or suffer from pain. The next day she woke up with a headache and did not feel well. The sight of her right eye was still affected. During the forenoon of June 12 she became quite blind and was taken to the Central London Ophthalmic Hospital where she was examined by Mr. H. P. Gibb, who referred her to Dr. Grainger Stewart. On examination she stated that she could not see and that she did not perceive the light of an electric torch which was moved in front of her. Her pupils were equal and reacted readily to light and on convergence. Examination of the fundus oculi revealed no abnormality. She was quite intelligent and gave a good history of her

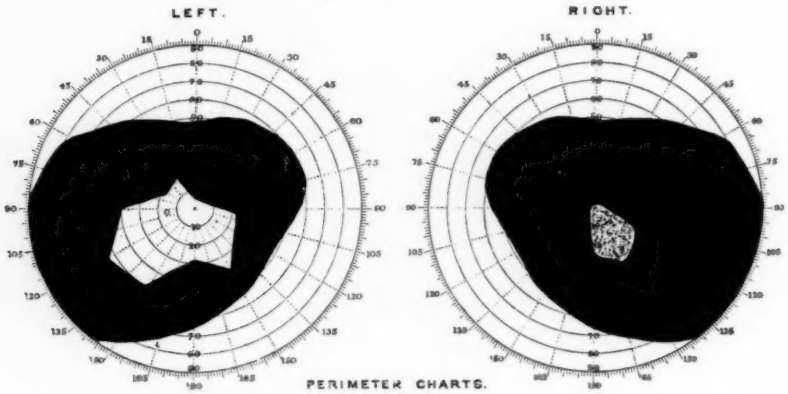


FIG. 4 (*Case* 3).—The left visual field was taken with a white disc 1 cm. in diameter; the right with a piece of white paper 10 cm. square.

previous health and of the onset of her illness, but she looked desperately ill and worn out.

Physical examination revealed no sign of local disease in the nervous system, and there was no evidence of any organic disease in her other organs. Her temperature was normal and her respirations regular and natural. As she appeared to be very ill she was sent to the National Hospital where she was admitted the same afternoon.

Examination at the National Hospital on June 13. The patient had had a good night but was dull and slow, although not confused. Her memory was impaired. On testing her vision she could distinguish hand movements with the right eye at 1 metre, and could read $\frac{6}{60}$ with the left eye. The field of vision of the right eye appeared to be more affected on the nasal side than on the temporal. There was no evidence of restriction of the visual fields of the left eye. The cranial nerves were normal. There was no speech defect

or sensory loss. The motor system was normal except for some weakness of the movements of both shoulders; the action of the diaphragm was impaired, but she did not complain of dyspnœa. The deep and superficial reflexes were all present and normal. She was unable to pass her water but had incontinence on coughing. Temperature 97·4° F., pulse 84, respiration rate 20 per minute.

June 14: Visual fields: in the right eye she appeared to have vision in the lower temporal quadrant only. The left side showed a horizontal hemianopia not quite complete in the upper temporal quadrant (fig. 4). Temperature 97·8° F., pulse 72, respiration rate 20 per minute.

By June 15, she had become very stupid and dull. She complained of severe headache and vomited occasionally. Her speech was slow but distinct, and she felt death impending. She practically never moved in bed. She was now completely blind, so that even a strong light was not appreciated, but she said that she had a greyish-white sensation in front of her eyes.

Ophthalmoscopic examination by Mr. Leslie Paton revealed a similar condition in both fundi. The discs were hyperæmic and swollen about 1 dioptre, and their edges were blurred. The veins, especially those in the lower half of the retina, were considerably distended. The condition was recognized as being a "true optic neuritis with papillitis," not a papilloedema. The pupils did not react even to flashes of strong light. The tendon reflexes were present, but the abdominals were absent and the plantars were of the Babinski type.

A lumbar puncture was performed and clear colourless cerebro-spinal fluid obtained which contained only two cells per cubic millimetre and 20 mg. protein per 100 cubic centimetres. The Wassermann reaction was negative both in cerebro-spinal fluid and blood. Temperature 98° F., pulse 72, respiration rate 20 per minute

During the next two days she became steadily worse.

The temperature, which up till then had been normal, rose during the night of the 17th-18th up to 102·8° F.

On the morning of June 18 she was semi-comatose, cyanosed and struggling for breath. The cyanosis and dyspnœa were temporarily relieved by oxygen, but respiration became more difficult and finally ceased, the pulse remaining strong up till the end.

Pathological examination.—A post-mortem examination was performed eighteen hours after death. The body was well nourished and there was no external evidence of disease. The lungs were congested at their bases, and in the right lung there was also early broncho-pneumonia. There were no pleural adhesions and no evidence of tuberculosis was found. The heart was healthy, and the aorta showed only the earliest stages of atheroma. The liver was yellowish with early fatty change in the centres of the lobules. Both kidneys showed slight fœtal lobulation; the capsules were slightly thickened and milky in places, probably owing to the pressure of corsets, but no abnormality was seen on section or microscopically. The suprarenals, uterus and ovaries were healthy.

In the brain there was slight general flattening of the convolutions, and a definite pressure cone was found in the foramen magnum. The cord presented no external abnormality except slight swelling in the upper cervical region. The optic nerves were removed, the right up to the lamina cribrosa, the left including the disc head and a small area of retina around it. The sphenoidal, ethmoidal and frontal air sinuses were examined and found to be healthy.

The brain was cut at the time of the post-mortem examination by coronal section just in front of and just behind its attachment to the brain-stem, without the discovery of any tumour or disease process. After hardening, however, further sections made in the coronal plane towards the occipital poles revealed

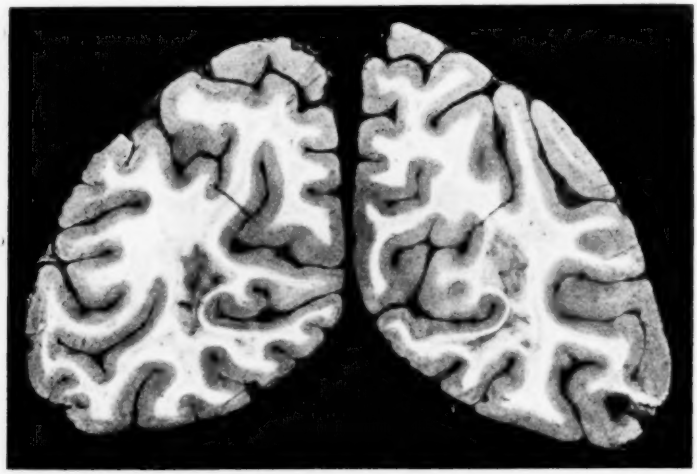


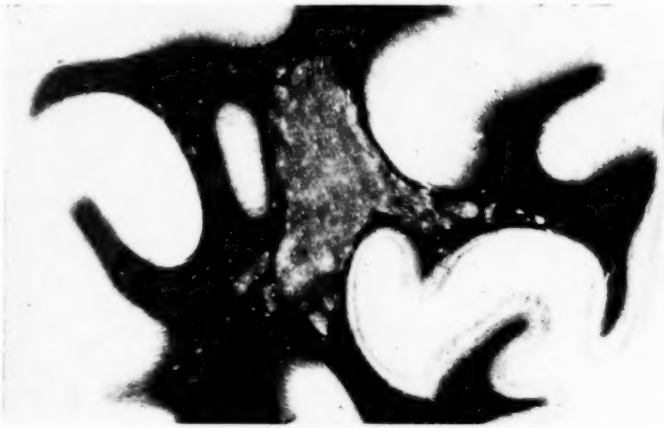
FIG. 5 (*Case* 3).—Coronal section across occipital lobes, showing symmetrical areas of degeneration.

areas of reddish discoloration and slight softening just external to the deep part of the calcarine cortex (fig. 5).

For the further examination of the brain, the brain-stem was first removed by a horizontal section above the superior colliculi, and was cut in serial horizontal sections 5 mm. in thickness. Frozen sections were first made from each block and the remainder was embedded in celloidin. The cerebral hemispheres were cut in serial coronal sections of the same thickness. Some pieces from the affected region of the occipital pole were cut by frozen sections, while others were embedded in celloidin. The following methods were employed: On frozen sections, Weigert-Pal, Bielschowsky, Cajal's gold sublimate method, Anderson's Victoria blue method for neuroglia, and Scharlach R. with hæmatoxylin. Of the celloidin blocks of the brain, several from various regions of the hemispheres were mordanted and stained by the Weigert-Pal method, and

others were embedded without mordanting and stained by iron-hæmatoxylin and Van Gieson's counterstain, and by toluidin blue. Similar methods were used for the brain-stem and cord, but the latter was too much softened in the affected region to allow of frozen sections.

Distribution of the lesion.—The areas of degeneration in the occipital poles were roughly crescentic in outline, or more exactly were shaped like the blade of a chopper. Their outer rounded margins reached about half way across the central white matter, and they were moulded round the deep part of the calcarine fissure from which they were separated by a thin zone of intact subcortical fibres. They measured 2·3 cm. in vertical and 1·7 cm. in greatest transverse diameter. In shape and size they were practically symmetrical, but that on the left side extended a little further back towards



MARINE BIOLOGICAL LABORATORY WOODS HOLE MASS. LIBRARY

FIG. 6 (*Case* 3).—Weigert-Pal section of lesion in occipital pole. The perivascular arrangement of the lesion is clearly seen. The white fibres forming Gennari's stripe are present.

the occipital pole, while that in the right hemisphere reached rather further forwards. They were not seen in front of a section cut 5 cm. from the occipital poles.

Two much smaller rounded areas were seen in the right hemisphere, one, measuring about 4 mm. in diameter, just under the cortex of the upper end of the ascending frontal gyrus, and the other, which measured only 2 mm., near it, but rather deeper in the ascending parietal gyrus.

The brain-stem and pons appeared normal to the naked eye, but a rounded area of degeneration was found in the right middle cerebellar peduncle, just lateral to the pons.

The cervical region of the cord was swollen and rather softened in its right half. This swelling extended almost throughout the cervical region, and in some segments involved the whole width of the cord. Below it the white

matter immediately around the horns was acutely congested, the horns themselves appearing healthy.

By the Weigert-Pal technique it could be ascertained that with the exception of the regions previously observed there was no gross degeneration of the white matter of the cerebral hemispheres. Particular attention was directed to the optic radiations but no degeneration of their fibres could be seen except in the occipital poles. There was, however, some early degeneration of individual fibres in the posterior limb of the internal capsule.

In the areas in the occipital lobes which have already been described the demyelination was severe and extensive but nowhere complete, as even in the centre of the area a few straggling irregular myelin sheaths could be seen. Many were beaded and some appeared to terminate in balls of degenerated myelin. It was obvious also from the appearance of the edges of each area that the demyelination commenced as a small rounded area centred on a blood-vessel and that the large areas were formed by the fusion of such small ones (fig. 6).

In the brain-stem several areas of degeneration not previously observed became evident by this method of staining. In the mid-brain a rounded patch of almost complete demyelination measuring about 5 mm. in diameter appeared in the fibres of the superior peduncle just below and external to their decussation. Below this, in the upper half of the pons, there were numerous small rounded areas, irregularly scattered through the ventral part of the pons. Each of these areas was centred on a small vessel the wall of which was infiltrated with small round cells (fig. 7). In the centre of each area the demyelination was complete, but the boundary between healthy and demyelinated tissue was not quite so sharp as in disseminated sclerosis. At a rather lower region in the pons these perivascular areas became grouped into a tri-radiate figure, one limb of which passed along the median raphe from near the ventral surface to the posterior longitudinal bundle, and the other two limbs passed forwards and outwards from the dorsal extremity of the central limb, at an angle of 30°, but did not quite reach the ventral surface of the pons. The area of demyelination in the right middle cerebellar peduncle was much larger than any other in the brain-stem, but the demyelination in it was not so complete as in the pontine areas.

In the medulla no demyelinated areas were visible, but a few fatty globules were intermingled with the fibres of the pyramidal tracts. In the cord there was a diffuse pallor and swelling of the right antero-lateral column which began in the lower part of the first cervical segment and spread down to the fifth, being most intense at the level of the fourth cervical segment. It disappeared in the sixth but reappeared in the seventh and eighth segments, where it affected the whole of the right antero-lateral part of the cord including the anterior horns. In the first thoracic segment very little abnormality could be seen, nor could any degeneration be traced in the lower segments of the cord. In the affected segments there was nowhere complete demyelination, but with higher powers of the microscope the myelin sheaths in the damaged areas were seen to be

swollen and broken up, and many compound granular corpuscles containing fatty material which took the Weigert-Pal stain were scattered through the tissues or collected around the vessels.

In sections stained by Bielschowsky's technique the axis cylinders were found to be relatively little affected in degenerated regions. They were less regular than normal, being thinned at one place and swollen in another. Often they appeared beaded or broken, but they formed a fairly complete network throughout the damaged area. This method also showed the nerve-cells and fibre systems of the cortex and the nerve-cells of the brain-stem to be substantially intact. The intracellular neurofibrils stained well, and there was little, if any, shrinkage of the cell bodies.

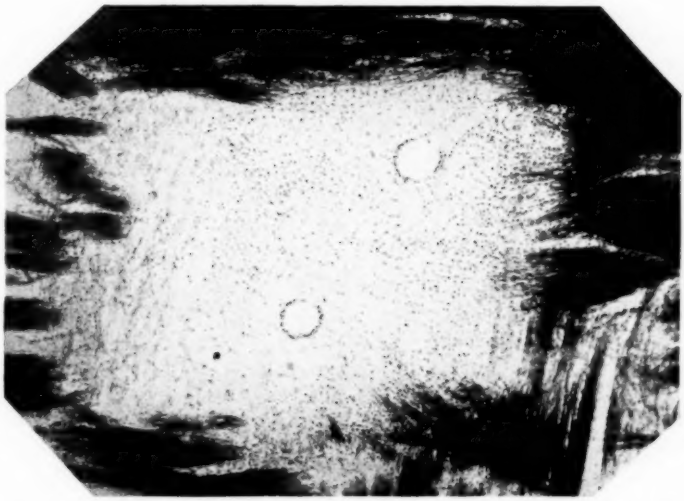


FIG. 7 (*Case* 3).—Section of lesion in pons (Weigert-Pal and carmine) showing the distribution of the demyelinated area around small vessels, the walls of which are infiltrated with small round cells.

Neuroglial and inflammatory changes.—It will be most convenient to describe the changes in the supporting tissues in the various degenerated areas together, since, although they varied in intensity from one place to another, they were all of the same nature. They consisted in: (*a*) small-celled infiltration with lymphocytes and plasma cells; (*b*) the presence of compound granular corpuscles and rod cells; (*c*) degenerative and regenerative changes in the neuroglia.

(*a*) It may be said at once that in all the affected regions perivascular infiltration with small round cells and plasma cells was found. It was very severe in the pons and cervical cord, where fairly thick cuffs of these cells were

seen round most of the vessels traversing the affected areas (fig. 8). In the occipital lobes, and in the two small areas on either side of the fissure of Rolando it was not so intense, but was obvious enough. The proportion of plasma cells varied from one area to another and even in different parts of one area, and clusters of plasma cells were encountered in several places either surrounding small vessels or apparently free in the nervous tissue. In such clusters it was not uncommon to find one or more binucleated plasma cells. In Nissl sections these clusters of plasma cells could be picked out with a low power objective owing to the large size of the cells and the metachromatic

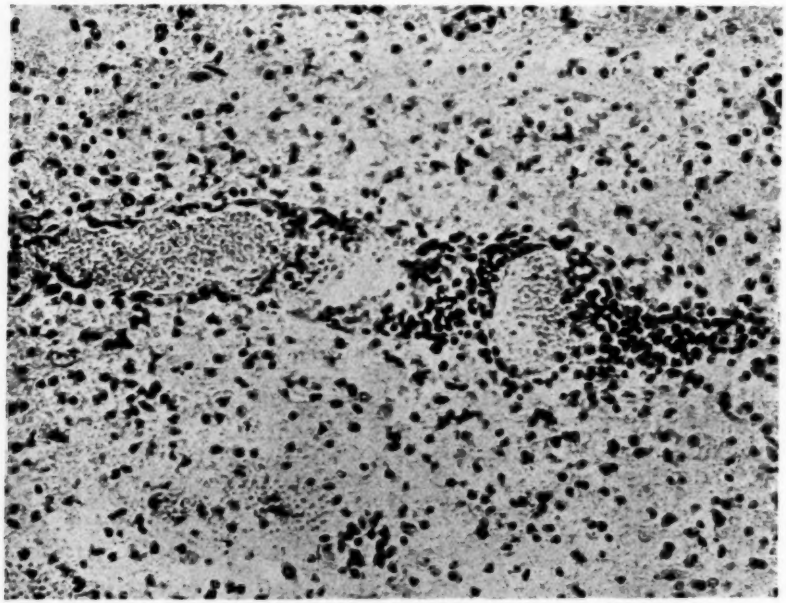


FIG. 8 (*Case* 3).—Cervical region of cord, showing perivascular infiltration, distension of vessels and minute hæmorrhages.

staining of their cytoplasm. The other small round cells corresponded closely to the lymphocytes of the blood, but it was not found possible to establish this definitely.

(*b*) Granular corpuscles were numerous in all the affected areas, but especially so in the brain-stem and cord. In the occipital poles they were limited to the neighbourhood of vessels, and in frozen sections stained with Scharlach R. did not form a very prominent feature. In fact in these sections there appeared at first glance to be very little except a general rarefaction of the myelinated fibres. Very few granular corpuscles were seen within the perivascular spaces,

most of these cells lying at a short distance from the vessel or against the outside of its connective tissue coats. This was true in all the areas examined, and may have been accounted for by the shortness of time which must have elapsed since the onset of demyelination. The contents of most of the granular corpuscles were not doubly refractile, nor did they take a very red stain with Scharlach R. They appeared indeed to be closely related to the myelin from which they were derived. A few doubly refractile crystals or dots were however seen, indicating a breaking up of the myelin into cholesterin-containing lipoids.

Rod cells were nowhere very numerous, nor were their nuclei so long or their cell bodies so obvious as in general paralysis. An attempt to stain the cell bodies and processes by Hortega's method failed, probably owing to the nature and length of the preliminary fixation. But the nuclei appeared very similar to those pictured by Hortega as found after a few days of subacute inflammation of the brain. In addition to these early rod cells, which were definitely pathological in appearance, there was an increase in the numbers of small round nuclei belonging either to the microglia or more probably to the oligodendroglia (interfascicular glia). This was most easily seen in the very small areas of degeneration near the vertex of the brain, and also in the cervical cord, since the line of demarcation between normal and affected tissue was here fairly sharp. Viewed under a fairly low power these areas stood out by the greater number of small nuclei which they contained, only a small proportion of which belonged to granular corpuscles. In the pons, and to a less degree elsewhere, there was evidence of slight swelling of the cell bodies of these interfascicular glial cells, and of the formation of mucin droplets in their cytoplasm, but the amount of mucin demonstrated by muci-carmine staining was considerably less than in Case 2.

(*c*) The changes in the fibrous neuroglia cells were more often degenerative than reparative. This is an inversion of the usual condition in non-septic conditions, and constituted one of the most unusual features of the disease. The most frequent change in the neuroglia cells was swelling of the cell body without formation of new fibres. This was associated with degenerative changes in the nucleus, which took one of two forms. Either the nucleus was swollen and generally pale, with a few rather large darkly staining dots round the periphery, or it had broken up into a number of rounded or rod-like bodies. The former change was the commoner and resembled the earlier stages in the formation of the so-called Alzheimer cells of hepato-lenticular degeneration, but no nuclei were so large as to be typical of Alzheimer cells. That the second change was due to karyorrhexis, and not to karyokinesis, appeared to be proved by its irregular nature, and by the fact that in areas where it was most common strongly basophil dots and rods, very similar to the nuclear fragments, were seen as inclusions in some of the endothelial cells of the vessels. Neuroglial cells showing karyorrhexis were not very numerous, although in several areas, especially in the mid-brain and cord, it was possible sometimes to see two such cells in a single high-power field.

Karyorrhexis in neuroglial cells has probably been frequently mistaken for mitosis, but there was no evidence that mitosis was occurring in this case. The appearance was always that of an irregular cluster of basophil knots in a rather swollen cell; no diaster forms were seen and binucleated neuroglia cells were very rare.

The reparative changes in the neuroglia cells were very slight and in the brain-stem they seemed to be altogether absent. In the occipital areas, however, a considerable number of enlarged astrocytes with strong processes could be seen by Cajal's gold sublimate and Alzheimer's fuchsin light green methods. These were only seen in the neighbourhood of vessels, and it

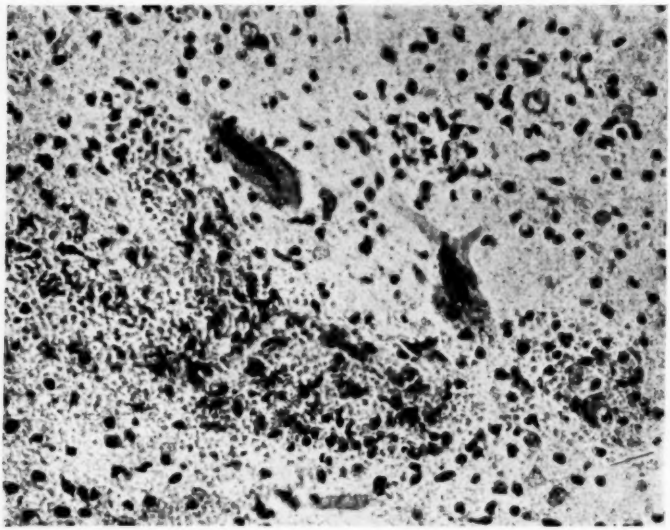


FIG. 9 (*Case* 3).—Spinal cord at seventh cervical segment. Area of hæmorrhage beside which two ventral horn cells are seen containing collection of black pigment granules.

was difficult to be certain that they were abnormal. In the cord also some large spider cells were found in relation to the heavier neuroglial septa, but these were not greatly removed from the normal.

Pigment in nerve cells.—Although the majority of the nerve cells, even in the affected areas, were healthy, there were two situations, the pons and the seventh cervical segment of the cord, in which many of the cells contained a black or dark brown, doubly refractile pigment (fig. 9). This pigment resembled in many ways that described by Claude and Loyez [3] as appearing in the nerve-cells in relation to recent hæmorrhages. In their cases they found it as early as forty-eight hours after the occurrence of bleeding. It has been found by us before in cases of hæmorrhage into and infarction

of the brain, and in this case also it occurred in association with small recent hæmorrhages.

In the cervical cord the large size and definite position of the anterior horn cells in which the pigment was found made it possible to study its solubility and other chemical relationships. The results of this examination agreed very closely with those obtained by Claude and Loyez. We found that it was insoluble in the cold in fat solvents, such as alcohol, alcohol and ether, xylol, chloroform and cedar-wood oil, and also in most acids, and that it did not give a Prussian blue reaction. It was soluble in ammonium sulphide and in weak alkalis, such as 5 per cent. sodium or potassium

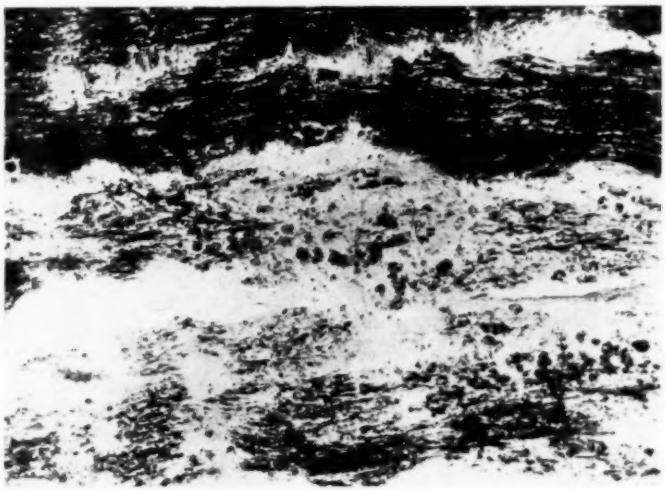


FIG. 10 (*Case* 3).—Optic nerve. Weigert-Pal section. Fragmentation of the myelin sheaths, and the collection of the fatty droplets in compound granular corpuscles are seen, especially in one bundle of nerve fibres.

hydrate, or 50 per cent. ammonia. It appears to agree in solubility with hæmofuscin, as given by Wells [13], and like it is decolorized in hydrogen peroxide. We found it to be soluble in xylol at 50° C., a fact which may explain the rarity with which it has been described, as it probably disappears during the process of embedding in paraffin.

From the histological point of view, as opposed to the chemical, its most important characteristic is a double refractility, so strong that the granules which appear nearly black under ordinary illumination stand out as bright specks under crossed Nicol prisms. This property distinguishes the granules at once from melanin, and allies them to the pigment formed by the malaria parasite, the larger granules of which at any rate are doubly refractile.

We have drawn attention to this pigment here in order to complete the histological description. A more complete study of it must be deferred for a later publication. If we accept the findings of Claude and Loyez its appearance in this case would indicate that the minute hæmorrhages in the pons and the cervical cord were at least forty-eight hours old, or at any rate that they did not occur immediately before death.

Optic nerves.—The *optic nerves* presented no macroscopic abnormality, but when stained by the Weigert-Pal method were generally paler than normal. On microscopic examination it was seen that very few of the myelin sheaths were intact. Most of them were beaded, and many were altogether destroyed, appearing as loose beads of myelin, or finer granules collected in the bodies

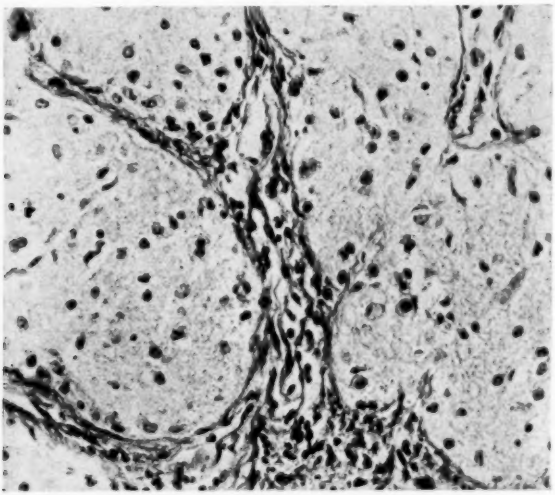


FIG. 11 (*Case* 3).—Optic nerve. Hæmatoxylin and van Gieson. The section shows infiltration of pial trabeculæ, and the formation of compound granular corpuscles.

of compound granular corpuscles (fig. 10). Staining with Scharlach R. produced a similar picture, but rendered the large number of compound granular corpuscles more evident. Tissue stains, such as Alzheimer's fuchsin light green and hæmatoxylin with van Gieson's counterstain, demonstrated an enlargement of the bodies of many of the neuroglia cells of the nerve, a change which appeared to be most intense immediately behind the disc head. Rod cells were also seen diffusely scattered through the nerve tissue. Altogether the nervous tissue appeared to contain many more cells than normal. There was also an excess of cells around the vessels in the connective tissue septa and in the meshes of the pia-arachnoid covering the nerve. Most of these were small round cells resembling lymphocytes, but a proportion of

plasma cells was also present. These cells nowhere formed a cuff, nor even a complete ring, round a vessel (fig. 11).

There was very little obvious difference between the two optic nerves, but they were certainly more affected towards their anterior ends than towards the chiasma.

Summary of Case 3.—A healthy woman, aged 43, became rapidly blind, first in the right eye and then in the left. This blindness was associated with papillitis, and later with hemianopia, which was roughly horizontal, affecting the upper half of both visual fields. She became stuporose, and died eight days after she gave up her usual work. At the post-mortem examination symmetrical areas of myelin degeneration were found in the white matter underlying the calcarine cortex. There was also some demyelination of the optic nerves, and areas of a similar character were found in the mid-brain, pons, cerebellum, and cervical cord. These areas had a perivascular arrangement, the larger being formed by the fusion of several small perivascular areas. The central vessels were surrounded with small round cells, among which there was an admixture of plasma cells. There was evidence of slight proliferation of neuroglial cells and fibres in the occipital areas and in more recent patches a few neuroglial cells showed karyorrhexis; some large pale cells resembling those described by Alzheimer in hepato-lenticular degeneration were also seen.

Discussion.

The pathological pictures presented by the three new cases which we report are so similar that there can be no doubt that they are cases of the same disease. The demyelination of the centrum ovale in all three cases had the characteristics of Schilder's form of encephalitis; it was symmetrical, it spared the subcortical band of white fibres, and it affected the occipital poles. These three characteristics have been emphasized by Collier and Greenfield [4] as being present in their cases, as well as in twelve out of twenty others abstracted from the literature.[1] In some cases it is true that in one or other characteristic the lesion was not quite typical. It might not be completely symmetrical, it might invade the subcortical arcuate fibres in isolated areas, and it might affect other regions of the brain more severely than the occipital lobes. But so far as these seventeen cases are concerned the gross pathological picture presents the closest similarity. In other details also our cases agree with those previously

[1] Our Cases 1 and 2 are referred to by Collier and Greenfield as "Blandy I and II."

recorded. Affection of the optic nerves, or at least of the chiasma, with papillitis similar to that in our Case 3, was described by Stauffenberg [11]. Lesions in the brain-stem were found in one of Bouman's cases [1], as in two of these here recorded, and a lesion of the spinal cord occurred in the case reported by Haberfeld and Spieler [6], as in our Case 3.

But the microscopic examination revealed changes which were so dissimilar that without the help of the gross appearances it would have been difficult to trace any relationship between them. The demyelination and destruction of axis-cylinders was the only point of resemblance, although it is true that the lesions in the pons in Cases 2 and 3 presented many similarities. In Case 1 the neuroglial reaction was intense, with a dense feltwork of fibres and many abnormal large forms of neuroglial cell. Perivascular infiltration was intense with the formation of thick cuffs of cells, and thickening of the adventitial tissue. In Case 2 there was little neuroglial overgrowth; no increase of fibres, or enlargement of cell bodies, was present, but there was an excess in the number of small interfascicular nuclei; and there was a complete absence of perivascular infiltration. In Case 3 the only neuroglial reaction seen was enlargement of some of the cell bodies, especially in the neighbourhood of the vessels, and karyorrhexis of a few of the neuroglial cells. Perivascular infiltration was definite, but not intense; plasma cells were found in this case, but not in the other two.

These differences may be to some extent at least associated with differences in length of clinical history, which was one to one and a half years in Case 1, four months in Case 2 and nine days in Case 3. It is noteworthy that the microscopic picture in Case 1 resembled very closely that described by Collier and Greenfield [4] in their second case, in which the duration of the disease was about the same. In our Cases 2 and 3 the cellular changes presented a greater similarity, and this may be correlated with the rapidly fatal relapse which occurred in Case 2, and with the very short history in Case 3. But it is probable that some part at any rate of the lesion near the vertex of the brain in Case 2 was of older date, as it probably accounted for the high stepping gait which was present for several weeks before death. It is possible that the disease was less acute in Case 2 than in Case 3, and therefore was not associated with such evidences of acute inflammation as perivascular infiltration, plasma cells and degenerative changes in the neuroglia cells.

On the clinical side other differences than that of length of history were found. In Case 1, which otherwise corresponded exactly to the typical picture of progressive cerebral blindness and mental deterioration, the first focal symptom was quite certainly deafness, due no doubt to a bilateral lesion of the temporal lobes.

In Case 2 there was no obvious loss of vision, and the case history is otherwise atypical.

In Case 3 the most striking feature was the extreme brevity of the illness and the very rapid deterioration of vision. The latter is only paralleled in the literature by the rapid blindness in the case of Rochon-Duvignaud, Jumentié and Valière-Vialeix [9]. This blindness was, no doubt, due largely to the affection of the optic nerves themselves, at any rate during the first few days. That the lesion under the calcarine cortex also played a part in it later on is suggested by the visual fields. In this case there was also quite definite evidence of increased intracranial pressure, as shown by flattening of cerebral convolutions and a cerebellar pressure cone. Increase of intracranial pressure has shown itself as an early symptom in the clinical record of several previously reported cases, but it appears to have receded rapidly. Its cause is probably either a local or a general cerebral œdema, due no doubt to the intensity of the toxic process occurring in the brain. At a later stage of the disease there is evidence that the brain shrinks to some extent, at any rate in the affected region.

Résumé of Recent Literature.

The cases reported up to 1924 have, with one or two exceptions, been analysed by Bouman and by Collier and Greenfield, and little needs to be added to this analysis. The only undoubted case of the disease to which they did not draw attention was one reported by Neubürger [8] in 1922 as "Disseminated Sclerosis in Childhood." Since the publication of their paper, cases have been reported by Urechia, Mihalescu and Elekes [12], by Flatau [5] and by Brock, Carroll and Stevenson [2]. A short analysis of these cases will be useful.

Neubürger, 1922.—A female child, aged 4½, became ill eight weeks before admission to hospital with weakness of legs, much crying and loss of vision. Ophthalmoscopic examination was negative. The pupils reacted slowly. The eye movements were good. The cerebro-spinal fluid was normal. There was at first increase of symptoms and intention tremor, then a remission, but later a relapse progressing to death. The total length of the illness was eighteen

months. On post-mortem examination of the brain the convolutions were shrunken, and on section *symmetrical* areas of gelatinous sclerosis were found in the white matter of the brain, especially in the occipital region, sparing the arcuate fibres under the cortex. The grey matter of the cortex and the basal ganglia were altogether spared. The author did not give an exact description of the size or number of the areas, but published a photomicrograph of a Weigert-Pal section which is typical of Schilder's encephalitis. Microscopically the most important observations were that the areas of sclerosis seemed to grow by the fusion of small perivascular areas, and that the axis-cylinders were destroyed in regions where the myelin sheaths were most affected. He figures enlarged "globoid" neuroglial cells similar to those described by Collier and Greenfield.

Urechia, Mihalescu and *Elekes*, 1924.—A male, aged 37, began to have headache in July, 1922. Towards the end of October he became depressed and suicidal. The gait became ataxic, with stamping of heels and some Parkinsonism. The cerebro-spinal fluid contained an excess of globulin and the upper normal limit of cells. Beyond diminution of the abdominal and ankle jerks no abnormalities were found on physical examination. He died from a bedsore in August, 1923.

Post-mortem: Numerous greyish gelatinous plaques were found in the brain, some very small, others measuring 2 to 4 cm.; they were almost entirely in the white matter and chiefly in the frontal lobes, but were found also irregularly scattered through the nervous system in the corpus callosum, basal ganglia, interpeduncular space, substantia nigra, dentate nucleus, pons and medulla. The authors state that in spite of great destruction of myelin sheaths the lesions of the axis-cylinders were slight, and that the transition from normal to sclerotic tissue was "brusque." Although the arcuate fibres were more resistant than the other white fibres of the subcortical zone, the areas of sclerosis in some places invaded the cortex, producing similar demyelination of the fibres in it. The cord was not examined.

The impression made on us is, that in spite of the atypical clinical history, this case was one of disseminated sclerosis, although the authors publish it as one of Schilder's form of encephalitis periaxialis diffusa. The pathological picture seems to approximate much more closely to that of the former than of the latter disease. No mention is made of symmetrical distribution of the plaques, the largest of which were only 4 cm. in diameter, and they were scattered irregularly through the brain-stem and possibly the cord. The illustrations given, particularly the Weigert-Pal sections of the pons and medulla, are typical enough of disseminated sclerosis, especially that of the pons, which shows asymmetrical demyelinated areas with sharply-defined edges.

Flatau, 1925.—A Jewish boy, aged 14, began to lose his sight in November 1920, and was completely blind three months later. Deafness had been observed some three or four months before there was any loss of vision. With the progress of the disease walking became impaired, and his mentality was altered so that he spoke little and only to complain of his blindness. On examination there was optic atrophy ; the pupils were unequal but reacted to light. The abdominal reflexes were weak, the plantar reflexes were of the normal type. He passed urine and fæces in bed. At first he could stand and walk unsteadily but without support, but this power was soon lost. He could taste and smell food and recognized objects by touch.

There were occasional convulsions, and he became progressively demented, retaining however the use of his hands and arms until near the time of his death in October, 1921. The length of history was thus eleven to fourteen months.

On post-mortem examination the brain showed microgyria of the occipital and parietal convolutions, and on section a diffuse gelatinous gliosis of the occipital and temporal lobes. The subcortical band of white fibres was invaded in parts of the occipital cortex but was spared elsewhere. Microscopically there was much gliosis with large astrocytes and compound granular corpuscles, but no perivascular infiltration and no plasma cells. The pyramidal tracts were degenerated throughout their length, and there was demyelination of the optic nerves and chiasma. This case is typical in its clinical and pathological features. From our point of view it is of interest in that deafness preceded blindness by a few months, just as it did in our Case 1.

Brock, Carroll and *Stevenson*, 1926.—A Jewish boy, aged 8½, in November, 1920, became irritable and fidgety, and developed intention tremor. His memory and sight became impaired. In March, 1921, he had a general convulsion, followed by general weakness, right-sided hemiparesis and difficulty in speech. At this time his hearing was normal. His right arm was ataxic, as was also his gait. In June there was right hemianopia with normal fundi. Both plantar reflexes were of Babinski type. A few days after this he became suddenly maniacal, and on recovering had convergent strabismus and right sided ptosis.

In December, 1921, he was completely blind, and his limbs and body were in an attitude of decerebrate rigidity. He died thirteen months after the onset of symptoms.

The lesion was chiefly occipital and was diffuse and typical.

If we exclude the case of Urechia, Mihalescu and Elekes, the other three cases present no new pathological features, except the demyelination of the optic nerves and chiasma in Flatau's case. Stauffenberg had found some demyelination of the chiasma in his case, but the nerves were not examined. In our Case 3 the demyelination of the optic nerves was seen in its earliest phases, and appeared to be a primary process.

On the clinical side two new symptoms are emphasized by these cases: (1) The occurrence of deafness as the first symptom. This was noted in our Case 1 also, and its association with a bilateral lesion of the temporal poles has been indicated; (2) attacks of mania during the course of the disease. Flatau's patient tore his bedclothes to shreds, and was very difficult to restrain in bed for several weeks. In the case reported by Brock, Carroll and Stevenson, the attack of mania was much shorter. This symptom is not surprising, though it is remarkable how seldom it occurs in organic disease of the brain, especially when, as in these two cases, the lesion is chiefly in the occipital and temporal lobes.

Diagnostic Criteria of Schilder's Encephalitis.

It may be asked whether it is possible to establish any hard-and-fast rules for the diagnosis of a disease which varies so much both in its clinical and its pathological features. The answer to this question must be in the negative. Undoubtedly many cases will always remain undiagnosed during life, and a few will still be in doubt after the most exhaustive histological investigation. It may even be asked whether the characteristic post-mortem appearances in the brain constitute a single disease, or whether they may result from a variety of causes. Although we are strongly of the opinion that the causative agent must be the same, or at least similar, in all the cases which present the typical picture, yet while we remain completely in the dark as to the nature of this cause, we are bound to reserve judgment.

It is, however, important to formulate some criteria for the differential diagnosis of Schilder's encephalitis from disseminated sclerosis. That this diagnosis presents difficulties in certain cases is evident from our review of the literature, for we have there included under the diagnosis of Schilder's encephalitis a case published by Neubürger as disseminated sclerosis. This author had reported a case of Schilder's encephalitis in the previous year, and was therefore quite familiar with the condition. We have excluded the case of Urechia, Mihalescu and Elekes as we consider it to be one of disseminated sclerosis.

The clinical records of our cases call attention to two symptoms of special importance, viz., loss of vision and loss of hearing. In Case 1, deafness preceded the onset of blindness, but it is to be noted that the

impairment of these senses showed no remission and resulted ultimately in total loss of hearing and of sight. In Case 3 the vision of one eye was affected before that of the other, but the second eye was affected within forty-eight hours, and in a few hours the patient was, apparently, completely blind, at any rate she stated that she could not see light. During the next two days it was evident that the sight had not completely gone, but on the fifth day of her illness she was completely blind. Whether she would have recovered her sight if she had survived is certainly doubtful when we take into consideration the pathological changes which were found in the optic nerves and occipital poles.

In these cases there was a progressive and ultimately a total loss of vision and hearing. In disseminated sclerosis vision may be impaired or lost, but as a rule one eye only is affected and recovery, usually complete, takes place within two to six weeks. It may sometimes happen that years after the occurrence of the temporary affection of sight the vision becomes again impaired, but it is rarely lost, and when this occurs definite pallor of the disc is seen on ophthalmoscopic examination.

Complete deafness is never met with in disseminated sclerosis except as the result of an independent ear affection, but unilateral impairment of hearing is not unknown. The progressive character and severity of these symptoms in Schilder's disease is in striking contrast with what is met with in disseminated sclerosis. This steady progression with increasing disability from the early stages is a feature commonly met with in Schilder's disease. On the other hand in disseminated sclerosis remissions and recurrences are the rule in the early stages of the disease.

Most cases are clinically quite distinct, but, as is only natural when the pathological changes in both diseases are so similar, others would seem to vary only in their acuteness and severity.

Pathologically, there can be no doubt that the diseases resemble one another in many particulars, and in very early cases, as our Case 3, it may be impossible to be certain of the diagnosis. It might be argued that this was a case of disseminated sclerosis in which the plaques in the brain and in the pons happened to be more or less symmetrical. The formation of demyelinated areas by the fusion of small perivascular foci which occurred in this case, is, however, unlike the lesion of disseminated sclerosis. But in cases of longer standing careful histological examination should clear up all doubt. The chief criteria here are,

firstly, the sharpness with which the plaques are defined, and secondly, the degree of preservation of the axis-cylinders. For the first of these the description given to the plaques by Nageotte and Riche [7] as "découpés comme à l'emporte-pièce" (as though cut out with a punch) is practically always true of disseminated sclerosis, and very rarely describes the plaques in Schilder's encephalitis. Still more important is the second criterion, since Schilder's encephalitis is not truly periaxial except in the earliest stages, and very soon entails destruction of the axis-cylinders and consequent Wallerian degeneration of the peripheral part of the fibres. An examination of the spinal cord and brain-stem will therefore enable the diagnosis to be made in almost every case.

SUMMARY.

Three new cases of Schilder's form of encephalitis are described. The patients were aged 8, 3 and 43 years, and the length of disease was eighteen months, three months and nine days.

In Case 1 the first symptom was deafness, and this was also true in a case recently reported by Flatau.

In Case 3 the initial blindness was associated with papillitis and was due to demyelination of the optic nerves. It is probable that the lesion in the optic nerves is similar to that in the brain.

In the differential diagnosis between Schilder's encephalitis and disseminated sclerosis the chief clinical criteria are the nature of the loss of hearing, and the progressive and complete loss of vision. On the pathological side the symmetrical and diffuse nature of the demyelinated areas, and the destruction of axis-cylinders in them at an early stage, are points which help in distinguishing this disease from disseminated sclerosis. The similarity of the pathological picture may, however, be so close as to cause erroneous histological diagnosis.

REFERENCES.

[1] BOUMAN, L. "Encephalitis Periaxialis Diffusa," *Brain*, 1924, **47**, 453.

[2] BROCK, S., CARROLL, P. M., and STEVENSON, L. "Encephalitis Periaxialis Diffusa of Schilder," *Arch. of Neur. and Psych.*, 1926, **15**, 297.

[3] CLAUDE, H., and LOYEZ, M. "Étude des pigments sanguins et des modifications du tissu nerveux, &c.," *Arch. de Méd. expér. et d'Anatomie path.*, 1912, **24**, 517.

[4] COLLIER, J., and GREENFIELD, J. G. "The Encephalitis Periaxialis of Schilder," *Brain*, 1924, **47**, 489.

[5] FLATAU, ED. "Encephalo-leucopathia scleroticans progressiva," *L'Encéphale*, 1925, **20**, 475.

[6] HABERFELD and SPIELER. "Zur diffusen Hirn-Ruckenmarkssklerose im Kindesalter," *Deutsch. Zeitschr. f. Nervenheilk.*, 1910, **40,** 436.
[7] NAGEOTTE, J., and RICHE, A. In CORNIL and RANVIER. "Manuel d'histologie pathologique," Paris, 1907.
[8] NEUBURGER, K. "Zur Histopathologie der multiplen Sklerose im Kindesalter," *Zeitschr. f. d. ges. Neur. u. Psych.*, 1922, **76,** 384.
[9] ROCHON-DUVIGNAUD, JUMENTIÉ and VALIÈRE-VIALEIX. "Cécité à marche rapide avec stase papillaire moderée," *Rev. Neurol.*, 1923, **30** (ii) 78.
[10] SCHILDER, P. "Zur Kenntnis der sog. diffusen Sclerose (über Encephalitis periaxialis diffusa)," *Zeitschr. f. d. ges. Neur. u. Psych.*, 1912, **10,** 1.
[11] STAUFFENBERG. "Ein Fall von Encephalitis periaxialis diffusa," *ibid.*, 1913, **39,** 556.
[12] URECHIA, C. I., MIHALESCU, S., and ELEKES, N. "L'encéphalite periaxialis diffuse, type Schilder," *L'Encéphale*, 1924, **19,** 617.
[13 WELLS, H. G. "Chemical Pathology," 5th edition, 1925, W. B. Saunders Co., Philadelphia and London.

MANGANESE TOXÆMIA; WITH SPECIAL REFERENCE TO THE EFFECTS OF LIVER FEEDING.

BY J. R. CHARLES, M.D.,

Physician to the Royal Infirmary, Bristol.

MANGANESE if absorbed in excess, as it may be in certain industrial occupations, produces very characteristic clinical manifestations.

At the commencement the patient complains of lack of energy and mental languor, with a feeling of bodily fatigue on exertion, which is probably due to an excessive amount of energy required to execute movements owing to the hypertonic condition of the antagonistic muscles when any movement is carried out. Another very early and characteristic symptom is emotional instability. This shows itself in a very great tendency towards the expression of amusement. I have seen no cases in which there has been a tendency to weeping, or an expression of despondency, but on the other hand excessive smiling without any adequate cause is very common, and the patient, if asked any simple question, will not infrequently burst out into hilarious laughter. When several of these patients are together they frequently gurgle with apparent amusement, as though they lacked emotional restraint. Their faces at rest show a Parkinsonian mask, although sometimes on this is superimposed a set spastic smile (figs. 1 and 2). The voice is almost invariably somewhat low in tone and monotonous.

Automatic movements of the limbs are in almost complete abeyance in advanced cases. There is a marked rigidity in all the muscles of the limbs and trunk. The arms are held to the sides and the forearms slightly flexed. Owing to the rigidity of the trunk muscles patients tend to fall like a straight pillar if pushed backwards or forwards (fig. 3).

Another very peculiar feature which the patients exhibit is the tendency, not only to walk with a stiff gait on a wide base, but also on their metatarsophalangeal joints, owing to a characteristic deformity of the feet which arises in many cases (fig. 4). Propulsion or lateripulsion may be present, but retropulsion is more frequent, indeed this is almost constant in advanced cases. There is no atrophy, and no alteration in the electrical reactions of the muscles is found.

Tremors of a coarse type are seen in the head and limbs, which become very marked on fatigue. These vary from fine twitching of the hand to rhythmical movements of the head, limbs and trunk, but anything approaching cigarette rolling movement has not been seen in this series of cases.

Romberg's sign was not constant. No changes in sensibility were found to touch, pain, temperature, stereognosis or the sense of position,

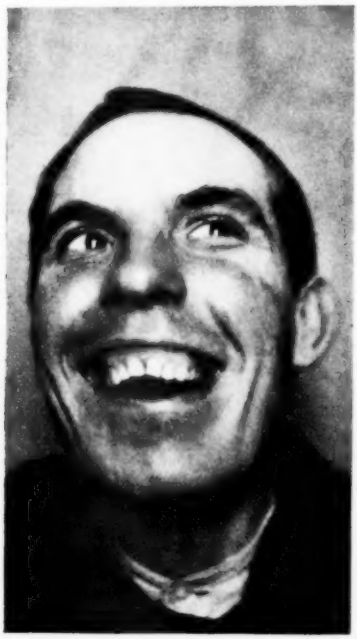


FIG. 1.—Showing hilarious expression without adequate cause.

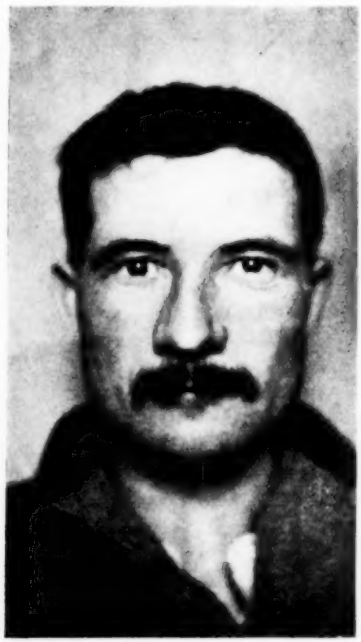


FIG. 2.—Showing set spastic smile.

but the patients almost invariably complained of cramp in their limbs, more particularly in the calves, which was worse after exertion.

Salivation may be increased. Sweating, particularly at night, occurred not infrequently.

The deep reflexes are increased. The plantar reflexes remain flexor in type, though in two cases an extensor movement of the great toe was observed as an intermittent phenomenon.

No abnormal changes have been met with in the cranial nerves, pupils, fundi or sphincters, and no abnormality was discovered in the urine.

Manganese occurs in very small quantities in the human body, 0·5 to 2·5 mg. of MnO being present in the blood, whilst small traces have been found in the hair, bones and milk.

Eleven cases have come under my observation during the last four

FIG. 3.—Showing tendency to fall as a straight pillar.

years, and although these varied in degree, they all presented a remarkably similar train of symptoms.

G. Marshall Findlay [2] has found that manganous chloride, if injected subcutaneously into animals, was extremely toxic to the parenchyma of the liver and kidneys, and that with small repeated doses this toxic action was chiefly exerted on the liver. He produced cirrhosis of the liver in rabbits, rats and guinea-pigs by subcutaneous injection of manganous chloride, and also obtained the same condition by oral administration in rats. The type of cirrhosis was definitely

monolobular, and he pointed out that the clue to this action of manganous chloride on the liver might possibly be due to the fact that manganese salts are largely excreted by the bile.

There is a great similarity between many of the clinical manifestations of manganese poisoning and the symptoms of progressive lenticular degeneration, which disease is associated with monolobular cirrhosis of the liver. A curious feature has been the very slight degree of clinical manifestations produced by this cirrhosis during life, even when the pathological changes have been very marked.

Stanley Barnes and Weston Hurst [1] have described a series of

FIG. 4.—Showing characteristic deformity of feet.

four cases of hepato-lenticular degeneration in one family, which seems to prove conclusively that the nervous symptoms never occur until the liver has become grossly diseased. They conclude that the cirrhosis in this disease is the result of a series of attacks of acute hepatitis, and that some toxin is poured into the tissues intermittently, and further that this toxin has a selective action on the lenticular nucleus. They say that this toxin might be "either the primary alimentary one which escapes through the damaged liver where filtration capacity is in abeyance, or arise from the dying liver cells themselves. On the whole we favour the former alternative, seeing that in alcoholic and other forms of cirrhosis no nervous disease comparable with Wilson's type has ever been described, although histological appearance of the

final stages of the livers in alcoholic cirrhosis is so similar to that seen as the end result in Wilson's disease."

In some of the cases of manganese poisoning described below, there was evidence of hepatic inefficiency, as tested by the lævulose method.

As manganese, even when injected subcutaneously, leads to cirrhosis of the liver, the question arises whether there may not be some other explanation of the relation of the hepatic condition to that of the nervous degeneration.

It is possible that the normal liver may secrete some hormone which may act beneficially on the brain, and that when this is in abeyance the nervous degenerations and symptoms arise. With such a possibility in view seven of these cases were treated by liver feeding. The method employed was to give one to two ounces of pounded raw liver in the form of a sandwich daily. The patients appeared to tolerate this without trouble, and it produced no alteration in their blood-urea. The results of treatment were, on the whole, as perhaps might have been expected, disappointing in long-standing cases. In these there was little, if any, improvement, but in the early cases the effect appeared more promising.

A striking feature is that when a patient has improved after taking liver, this improvement has set in with remarkable rapidity, i.e., within the first few days of its administration, and this amelioration of the symptoms has been maintained while the patient continued the liver treatment. No case has been cured.

The suggestion is therefore made that the liver which has been taken supplies a deficiency of some hormone which may exert a vitalizing action on certain parts of the brain. If this is so, it might possibly restore function to cells which had lost their power for work but which were not irretrievably destroyed, through lack of such a stimulating substance. On the other hand, it would be quite impotent to restore the functions of cells which had lost their vitality.

In the first case treated, that of William W., the patient unquestionably made very great progress during his stay in hospital.

Case 1.—William W. was admitted December 3, 1925, complaining of inability to walk properly. Since August his gait had been like that of a drunken man.

Family history showed no nerve disease.

Previous history.—He has had the usual childish complaints. He served in the Army from 1917-1918; in France for two months, but he was not wounded and had no illness. Since January, 1920, patient had worked as a labourer in steel works, as a bricklayer's labourer in quarries, and on the road until 1925.

In April, 1925, he went to some manganese works as a labourer, and remained there until August, when he was discharged owing to the weakness of his legs. His work consisted of filling tubs with manganese powder. This powder falls down through a sieve and a funnel into a cask, and the patient's work was to press it down. Since August his legs have been weak, so that he rested when he walked. He ascended stairs with marked difficulty, and he walked forward on the balls of his toes. His appetite was good and he suffered from no gastric disturbances. He slept well, and his bowels were regular. No urinary trouble was present. He used to drink two pints of cider a week, but since August he had given this up and drank tea mostly. Since August he had had sharp shooting pains across his forehead, but after treatment these were better. He had no other pains or cramps, but he complained of generally feeling hot over his trunk and limbs, and of sweating at night and by day more than was usual for him.

On examination.—He was well nourished. He had a fixed unblinking expression. Emctional movements were almost absent, but voluntary movements of the face were good.

Nervous system: Memory was not good; he sometimes forgot words and places. Attention was fair, but he got "a bit muddled" if people talked to him too quickly. Articulation was thick, monotonous and slurred. Smell was not very good. Salivation was not marked; indeed, he said his mouth felt dry. His pupils reacted to light and accommodation. No nystagmus, strabismus, diplopia, or ptosis was present. His fundi, optic discs and visual fields were normal, and the functions of all the other cranial nerves were unaffected.

Motor system: Muscular power of his legs, which were in a state of extensor spasticity, was poor. No tremor was present and co-ordination was fair. No muscular hypertrophy and no atrophy was present, and dysdiadokokinesia was absent.

Gait: His legs were stiff, feet wide apart, and he leaned forward from the waist. Retropulsion, propulsion and lateripulsion were all pronounced. With his eyes shut he swayed considerably. He walked very definitely on his metatarsophalangeal joints. There was relative absence of automatic movements of his arms when walking. Although there were no definite areas of anæsthesia or analgesia, he was a little inaccurate in his replies to heat or cold stimuli all over the limbs and trunk, and also a little inaccurate in the localization of touch over the same areas.

Nothing abnormal was found in his lungs, heart, abdomen, or urine. The liver dulness was normal, and the edge could not be felt. His spleen was not palpable.

December 10: Lævulose test.—Fasting blood-sugar 0·109 per cent.; 50 grm. of lævulose given.

½	hour	later,	blood-sugar	0·117	per cent.
1	,,	,,	,,	0·133	,,
1½	hours	,,	,,	0·117	,,
2	,,	,,	,,	0·112	,,

This indicated hepatic inefficiency.

On December 18, he was given 1 oz. of raw ox-liver, which was increased to 2 oz. on the following day.

On December 18, van den Berg's reaction of blood was investigated. This gave direct negative and indirect negative results (0·5 unit).

December 21, 1925: His muscle power was steadily improving. He was quite steady when standing with his eyes shut, and the tendency to retropulsion and propulsion was very slight. The improvement in this case was remarkably rapid and progressive, so that on December 30, his gait was steady and almost normal, although he still had a tendency to walk on his toes. He no longer walked on a wide base and could turn sharply and without trouble. His facial expression was more mobile. There was still an unnatural automatic immobility of his hands and arms.

January 6, 1926: His facial expression was still improving, his eyes had more expression. The eyelids moved when he was talking. He smiled naturally at times. His gait was still steady, and he was now able to run remarkably well.

On January 12 his blood-urea was 0·035 per cent.

January 14: He was quite accurate in the localization and appreciation of tactile heat, cold, pain and pressure stimuli. Stereognosis and sense of position were normal.

January 18: His speech was slow, a little thick and monotonous, but he continued to be able to run quickly on a normal base without any indication of spasticity, and he was able to turn normally and easily.

He was discharged on January 20, very greatly improved.

Case 2.—John B. was admitted to the Bristol Royal Infirmary on January 25, 1926. This was a long-standing case. He had previously been under my care at the Bristol Royal Infirmary in 1921, two years after he had left the manganese works, where he had worked seven months. Whilst he was there he found himself getting weaker, so that he could only walk with difficulty, and he gradually lost his voice. He could shuffle along fairly well on the level, but was obliged to go uphill on his toes, and when coming downhill went faster and faster until he ran into something or fell over. He had a great tendency to retropulsion. He spoke in a very low monotonous voice. There was a marked Parkinsonian mask; he was unable to whistle, and responded very defectively to emotional stimuli. His tongue was tremulous. Power was deficient in all the movements of his arms and legs, and his leg muscles were definitely spastic. His gait was dragging and spastic in type; he walked on a wide base and trod on his metatarso-phalangeal joints. When pushed gently backwards he fell like a rigid pillar. There was an absence of the normal automatic swing of his arms. The reflexes were all normal. He complained of a good deal of sweating in his back at night—a symptom frequently complained of by these patients.

While in the infirmary in 1921, his power of walking improved.

On January 25, 1926, when he was re-admitted, all the symptoms were much the same as when he was examined in 1921. His speech was low

and monotonous, and difficult to hear at any distance, being almost a whisper. His expression was one of perpetual pleasure. The nasolabial folds were very poorly marked, and he was unable to whistle or frown. He had marked tremor in his tongue on protrusion. His muscular power was poor, particularly in his legs, where the flexors were, however, stronger than the extensors. His feet were in a position of hyper-extension, though flexed at the metatarso-phalangeal joints (fig. 5). Hypertonicity was very marked in his legs, although not in the arms. He had no tremor except in his

FIG. 5.—John B., January 26, 1926.

FIG. 6.—John B., February 11, 1926.

tongue, and his co-ordination was good. His gait was most unsteady; he walked on his metatarso-phalangeal joints, with a wide base of 1½ ft.; he started slowly, then trotted forward in a shuffle until he fell forward or was brought up against a wall. His usual mode of locomotion was on his hands and knees, as being easier and safer. If pushed gently on the chest he fell backwards like a log. There was no localized atrophy. He complained of frontal headaches and also cramp in the calves of his legs at night. He felt hot or cold for no apparent reason, and occasionally complained of pins and needles in his limbs. There was no abnormal objective sensory disturbance. The deep reflexes were all normal. The right plantar reflex was flexor in type, the

left being rather indefinite occasionally, but not always, producing a slight extensor movement.

January 28: The urine contained 1·7 per cent. urea. 15 grm. of urea were given by mouth; one hour later the urine contained 1·8 per cent. urea; two hours later 3·4 per cent. Blood-urea 0·03 per cent. Van den Berg's blood reaction gave negative results, both direct and indirect (0·25 unit). One to two ounces of liver were given daily.

January 29: Lævulose test.—Fasting blood-sugar, 0·083 per cent. 50 grm. lævulose administered.

½	hour later,	blood-sugar	0·108 per cent.
1	,, ,,	,,	0·105 ,,
1½	hours ,,	,,	0·104 ,,
2	,, ,,	,,	0·101 ,,
2½	,, ,,	,,	0·094 ,,

On February 8, 1926, he was walking better and had more control over turning and altering his speed, and he could pull up sharply when walking. His voice was stronger. On February 10 he walked on the whole sole of his feet, placing his heels on the ground before his toes. He stood easily on the soles of his feet.

On February 13 the blood-urea was 0·041 per cent.

February 15: He was not so easily pushed backwards, and his voice could be heard twenty feet away, which was a great improvement.

February 23: He could now walk backwards and his gait was distinctly better.

Hepatic efficiency test: Fasting blood-sugar, 0·082 per cent.; 50 grm. lævulose given.

½	hour later,	blood-sugar	0·092 per cent.
1	,, ,,	,,	0·091 ,,
1½	hours ,,	,,	0·100 ,,
2	,, ,,	,,	0·09 ,,

Blood-urea 0·047 per cent.

On February 29, he could walk still better, at the rate of about 144 steps per minute.

March 17: He could run rapidly on a slippery floor, stop himself and turn round. This improvement continued and he was discharged on March 27.

This patient showed evidence of slight hepatic inefficiency. He was treated with raw liver and improved while taking it.

Case 3.—Harry F., was admitted to the Bristol Royal Infirmary on March 29, 1926, complaining of weakness in the feet, arms and voice. There was no history of any serious previous illness. He had been in the Navy until 1905. He began work in a manganese factory, grinding the metal, in 1919, and after about twelve months he noticed difficulty in walking and felt as if he had weights on his heels, which got worse so that he became rapidly exhausted on exertion. A little later he began to notice weakness in his voice, felt giddy and

staggered when at his work. When he lay down at night he noticed twitchings in both his legs. His voice became weaker, and last summer he lost it completely for two or three days. Then he noticed that he was unable to control himself from laughter without any adequate cause.

On examination.—He was well nourished and had a good colour, but the expression on his face was very distinctly fixed and of the Parkinsonian type. His memory and intellectual functions were all good. His voice was low, monotonous and rather husky; he was quite unable to raise his voice or to speak loudly. His words were rather indistinct and slurred. The pupils were equal and reacted normally. There was no nystagmus, strabismus, or diplopia. His fundi were normal too. His facial movements were all weak, and when asked to frown he did so with great effort and with a coarse tremor. There was also a good deal of tremor of his face when he was asked to raise his eyebrows. The movements of his lids were sluggish. His tongue was tremulous when protruded, but no other defect was found in the functions of the cranial nerves. There was some weakness of all the movements of his arms and legs, and a very noticeable absence of automatic movements when he walked. His base was wide and there was a tendency for the toes to turn under his feet as he walked. He trod on the outer side of his left foot, in which there was a marked hallux valgus. The same deformity was present to a less degree in the right foot. His sphincters acted normally. Propulsion, lateripulsion, and retropulsion were all present, but not in a very marked degree in this patient. He complained of his legs feeling cold at night, and also of a sensation of cold between his shoulder-blades. He suffered a good deal from headache, chiefly over the coronal suture. There were no changes in tactile, pain or thermal sensation, or in stereognosis. Often spontaneously, and also at any ordinary remark, his face would assume the appearance of marked laughter; he made little sound, but appeared to be convulsed with secret amusement. The deep reflexes were all normal and the plantar reflexes were flexor in type. The abdominal reflexes were present. Nothing abnormal was found in his chest, lungs, or abdomen. The liver appeared normal in size and the edge could not be felt. This patient was so easily convulsed with laughter when palpated that it made the examination very difficult.

Hepatic efficiency tests.—Fasting blood-sugar 0·090 per cent. 50 grm. lævulose given.

½	hour	later,	blood-sugar	0·120 per cent.
1	„	„	„	0·121 „
1½	hours	„	„	0·122 „
2	„	„	„	0·121 „

There was therefore evidence of hepatic insufficiency.

Blood-urea 0·067 per cent.

On March 30, he was put on 1 oz. of liver, which was increased to 2 oz. This patient made slight improvement. His walk became brisker, his voice stronger, and he said that he felt better in himself, but there was no very material alteration in his symptoms. He went out from the infirmary, at his own request, on May 22, 1926.

Case 4.—Wm. Wd., aged 25. In this case emotionalism, especially hilarity and uncontrollable mirth, was a very marked feature. Laughter was very easily elicited, and he had prolonged fits of quiet gurgling to himself.

The symptoms began in 1923, after he had worked about nine months in a manganese works, with pains in the upper arms and shoulders, especially in the right, which were dull and aching in character, but sufficiently severe to interfere with his sleep. These pains lasted nearly a year, when they gradually disappeared. He also suffered from giddiness and would stagger, or even fall unless he caught hold of something. Later he found he could not walk very far without getting abnormally tired. He had great difficulty in controlling his speed when he walked downhill, and loss of balance when he tried to turn. His voice became weak and he found great difficulty in speaking distinctly, more particularly when he used words beginning with the letter S. He stated that he had had some difficulty in swallowing, but this was not a noticeable feature when he was under observation.

On examination.—His head was held stiffly, slightly inclined forward. The lips were parted, exposing the upper and lower teeth, and there was a marked tremor visible in them, especially on the right side. His general expression was one of fixed pleasure. His intelligence was rather dull, and his memory for quite recent events was defective. When asked to repeat a simple sentence of eight words he only, as a rule, got as far as the fourth word. There was some oscillation of a nystagmoid variety in both eyes on lateral deviation to the left. He was unable to frown and could only just elevate his eyebrows. Tremor was present in the upper eyelids, especially when they were slightly closed. The movements of his mouth were poorly executed and there was a very distinct tremor in his lips. There was also a considerable tremor in the left shoulder when he attempted to shrug it, and a good deal of tremor in the tongue on protrusion There was a considerable loss of power in all the movements of both arms, though the right was more feeble than the left. Interosseal movements in each hand were particularly poor. His grips were very weak and all the movements in the arms could be prevented with ease. This was also true, though to a lesser degree, in the legs. The head movements were considerably modified; there was but little antero-posterior voluntary movement. The jaw was very easily prevented from moving. The leg movements were also coarsely tremulous, in fact there appeared to be a generalized tendency towards tremor, which was particularly obvious when the patient was not thoroughly warm. His gait was peculiar, he took relatively long strides forward; there were exaggerated movements at the knees, the feet being picked up well from the ground during the initial part of the step, but during the latter part the feet slipped along the ground with a shuffling movement, the toes meeting the ground first. The axis of the trunk was inclined slightly forward, and there was a tendency to gain speed. The arms were partially flexed all the time, and the elbows somewhat abducted. Turning was usually effected by heaving himself round when he got hold of some rigid structure, but could be very cautiously executed without assistance in this way. He could stop

himself, but not abruptly. Retropulsion, propulsion and lateripulsion were all exhibited. The majority of the limb muscles were flaccid. The whole of the left sternomastoid appeared to be in a state of partial contraction, and its sternal attachment was unduly prominent compared with that of the other side. There was no atrophy, and no objective or subjective sensory disturbances. The deep reflexes were all brisk, the knee-jerks being exaggerated. The abdominal reflexes were normal and both plantars were flexor in type. The liver dulness was normal, and the edge could not be felt. Nothing abnormal found in the abdomen.

On March 26, 1926, the hepatic efficiency test carried out: Fasting blood-sugar 0·09 per cent. 50 grm. of lævulose were given.

½ hour later,	blood-sugar	0·09 per cent.
1 „	„	0·095 „
1½ hours „	„	0·095 „
2 „	„	0·095 „

He therefore showed no evidence of any inefficiency.

He was, however, given liver. Blood-urea on April 16, was 0·068 per cent. He made slight but definite improvement, and in May was able to run. There was, however, little improvement in his gait. He left the infirmary in August without having derived any material benefit.

His face presented an almost constant expression of extreme amusement (fig. 1).

Case 5.—S. H. W. A long-standing case dating from 1915. He complained of dull pains in the joints of his thighs and legs, and dull vertical headache. Articulation was very low, without power, and monotonous in character. There was marked weakness of his face, inability to frown, and he could smile with difficulty only. All the movements of his arms and legs were very weak, and especially those of his legs. He was first seen by me in 1921, when he had a typical Parkinsonian face, and a fine tremor in his tongue on protrusion. At that time he had no loss of power in his arms, but much weakness and spasticity in his legs, being able to walk with the greatest difficulty and a support; he usually shuffled along with two sticks. He put his foot forward on his metatarso-phalangeal joints, and walked on a broad base. He had a great tendency to fall backwards like a rigid pillar when pushed, and had the greatest difficulty in turning. His condition, in 1926, was much the same, but his arm movements were now weaker. His knee-jerks were exaggerated on both sides, and double ankle-clonus was present, but the plantar reflexes were flexor. There was no objective sensory defect. He found it very difficult to walk on the slippery floor of the ward, and fell down twice, bruising his knees.

On February 24, 1926, the blood-urea was 0·025 per cent. The hepatic efficiency test carried out on March 2, 1926: Fasting blood-sugar, 0·099 per cent. 50 grm. lævulose were given.

½ hour later,	blood-sugar	0·105 per cent.
1 „	„	0·097 „
1½ hours „	„	0·093 „
2 „	„	0·089 „

In spite of the fact that these figures showed no evidence of hepatic inefficiency, the patient was treated with liver from February 12 to April 19, but made no improvement worthy of note.

Case 6.—F. J., aged 42. Another case of manganese poisoning. This patient had been employed shovelling the ore into a machine for sieving for three years previous to 1919. Since this time he had been disabled, and was therefore a long-standing case. He showed much the same group of symptoms as the others. He had a very mask-like expression of face, but in his case there was very little response to emotion. His tongue was tremulous, and he spoke in an undertone with a monotonous voice. He complained of cramp-like pains in his calves at night, and a feeling of coldness in his legs and feet. The muscles of his legs, and to a less extent those of his arms, were weak, more particularly the left. His gait was spastic, his feet were placed wide apart, his toes coming to the ground before the heels, in fact his heels barely touched the ground. His arms were rigid and adducted to his sides when walking, and presented no automatic movement. This patient had an extensor plantar reflex on the right side, but the case was probably not an uncomplicated one of manganese poisoning, as there was a previous history of venereal disease. He had been under my care in 1919 with spastic paresis of his legs, increased knee-jerks and an extensor plantar response on the right side. He was given injections of N.A.B., and was discharged at that time with much improved gait, although he had strongly positive Wassermann reaction, which however was negative both in the blood and the cerebro-spinal fluid in 1921.

This patient was treated, like the others, with raw ox-liver, but made no progress under the treatment.

Case 7.—R. S., aged 21. This patient had a fixed expression with rather a vacant look. Voluntary smiling was performed with the greatest difficulty, but involuntary smiling was very easily elicited. He had prolonged fits of laughter from no apparent cause. He had a weak and monotonous voice with a tendency to slur his words, and he had recently developed a stammer. He gave up his work of grinding and sieving manganese in October, 1923, owing to weakness in walking, his trouble having started the previous August with staggering at his work and a feeling of giddiness, which necessitated his having to catch hold of some firm structure. In September his voice became affected, and he complained of cramp in the calves of both legs and some weakness in his left arm. Apart from his face, no abnormality was found in the functions of the cranial nerves. In this case there was a tendency for both feet to drop, particularly the left, and the left foot was held in an inverted position. There was very little spasticity, and no alteration in sensation. When walking he raised his feet unduly high from the ground, the left foot dropping into an extended position, so that the toe met the ground when the leg was carried forward. There was a slight degree of genu recurvatum. Propulsion, lateri-pulsion and retropulsion were very definite. All the deep reflexes were brisk. There was a tendency to an extensor right plantar reflex.

On April 20, 1926, the blood-urea was 0·053 per cent. Hepatic efficiency test carried out: Fasting blood-sugar, 0·101 per cent. 50 grm. lævulose given.

½ hour later,	blood-sugar	0·115	per cent.
1 „	„	0·112	„
1½ hours	„	0·093	„
2 „	„	0·121	„

The last figure is suggestive of food having been taken during the test.

This patient also went through a course of liver feeding, and although he walked steadily on discharge, it is difficult to say that he derived any material benefit from the treatment.

It will be seen from the above records that one early case made very great improvement while under treatment with liver feeding, and others apparently derived much benefit. These observations do not, however, conclusively prove that the improvement owed its cause to the liver feeding, as it is very difficult to eliminate the factor of suggestion, which may have played the predominant rôle in the treatment.

As far as possible this fallacy was guarded against, and it is perhaps worth noting that several long-standing cases, in which irrevocable damage had in all probability been sustained by the nervous system, derived no benefit whatsoever.

As a further safeguard, and to furnish controls, one case of post-encephalitic Parkinsonism and two of paralysis agitans were treated by the same method, at the same time, in the same wards. None of these manifested any amelioration of their trouble. Two cases of Sydenham's chorea were also treated by feeding with raw liver without any obvious effect. In the two cases of paralysis agitans the lævulose test revealed no evidence of hepatic inefficiency.

I am very much indebted to Dr. A. D. Fraser for carrying out all the pathological examinations.

Summary.

(1) Seven cases of manganese poisoning are described.

(2) The suggestion is made that the nervous phenomena are due to deficiency of a hepatic hormone.

(3) Treatment with liver was therefore adopted.

(4) Some benefit was obtained in a few cases.

References.

[1] Barnes, S., and Weston Hurst, E. W. *Brain*, 1926, **48**, 19.

[2] Findlay, G. Marshall. *Brit. Journ. Exper. Pathol.*, 1924, **5**, 92.

THE RELATIONSHIP BETWEEN THE STRENGTH OF THE CONDITIONED STIMULUS AND THE SIZE OF THE RESULTING CONDITIONED REFLEX.[1]

BY P. S. KUPALOV, M.D. (LENINGRAD),

AND

W. HORSLEY GANTT, M.D.

(From the Physiological Laboratory of Professor I. P. Pavlov, at the Institute of Experimental Medicine, Leningrad.)

FROM any indifferent stimulus it is possible to form a conditioned salivary reflex ("food reaction") in the dog. Such a stimulus must be above the threshold of excitation for the brain, and it must not give rise to any innate (unconditioned) reaction of greater potency than the unconditioned food reflex, e.g., a pain or a sexual reflex.[2]

When the conditioned reflex has been established, saliva begins to flow after a latent period of from two to ten seconds following the application of the stimulus. The measurement of the salivary flow is made as follows: A small glass balloon is fastened with wax to the salivary fistula. It has two outflow tubes, one of which is connected to a manometer outside the dog's cabinet, while the other and lower tube remains closed except when opened to allow of the syphoning off of the collected saliva.

The flow of saliva into the balloon increases the pressure in the system and causes a movement of the fluid in the horizontal manometer, one graduation of which corresponds to 0·01 c.c. of saliva. The quantity of saliva secreted is the measure of the potency of the conditioned stimulus.

STRONG AND WEAK STIMULI.

In the early investigations upon conditioned reflexes it was found that in a dog showing a salivary reaction to several conditioned stimuli one of the latter was more potent than the others. For example,

[1] Read before the Scientific Assembly of the Institute of Experimental Medicine, Leningrad, May, 1926.

[2] To supplant psychological by physiological terminology, it is the custom in Pavlov's laboratory to speak of a reflex to pain as a "reflex to destructive stimuli."

auditory stimuli: a metronome, an electric bell, or various musical tones, elicit a more speedy and abundant salivary response than do optical or cutaneous stimuli, such as flash-lights, images, scratching, &c. Least potent are thermal stimuli. On this basis laboratory stimuli were divided into strong (auditory) and weak (optical and cutaneous).

These differences were originally regarded as the expression of different intensities of stimulus. One may assume that in the case of sound stimuli there is a greater amount of external energy transported to the peripheral receptors than in the case of cutaneous or thermal stimuli, and that as a result a nervous impulse of greater intensity is sent into the central nervous system in the former case. That the conditioned reaction depends upon the strength of the acting stimulus receives direct confirmation in the laboratory. Thus, it has been shown (Tichimirov and Zelony [6], [8], [9]), that in the response to a certain tone there is a greater reflex effect when the strength of the tone is increased, the pitch remaining constant, and a correspondingly smaller effect when the tone is weakened. This is true for other stimuli in the same analyser. Kasherinova [2] proved this for tactile and Orbeli [3] for optical stimuli. Zelony found that if a conditioned reflex be formed on a chord of several tones, a single tone of the chord elicits a weaker response than the whole cord. In the case of a chord composed of two tones of unequal strength, of the two tones tried separately the stronger is the more potent as a stimulus. Thus there are a number of observations which indicate that the size of the conditioned reflex depends upon the physical strength of the stimulus. There are, however, other observations which suggest a relationship between stimulus and response of greater complexity than that outlined above. In the first place the application of weak stimuli, more particularly tactile and thermal, evokes a state of drowsiness in the animal. It is now possible to assert that the process of "internal inhibition" is the basis of the process of sleep, and, proceeding from this, we may suppose that the nervous elements of the skin and the thermal receptors of the cerebral cortex possess special functional properties. They cannot remain long in a state of excitation and pass quickly over into one of inhibition. Upon what factors this depends is too complex a question for discussion here.

On what does the difference in the size of the reflex reaction to stimuli belonging to different analysers depend? This difference was formerly explained as an expression of individual functional properties of the nervous elements of the different analysers in the cerebral cortex. It might be supposed, for example, that the nervous elements of the

tactile and thermal analysers cannot produce so strong a process of excitation as those of the auditory analysers, and that they more readily pass over into a state of inhibition. Such a view lacks experimental verification.

Certain observations suggest that the difference depends solely upon the strength of the stimulus, upon the amount of energy sent into the cortex. To investigate this problem we employed complex stimuli affecting several analysers. It was already known that in the reaction to a complex of two simultaneous stimuli the chief effect was produced by one of the components, that of the other being suppressed, so that the latter did not produce the reaction which it would have done had it been employed alone. If we assume that the magnitude and stability of the conditioned reflexes to auditory stimuli when compared with the responses to cutaneous and optical stimuli depend, not upon a qualitative difference in the nervous processes concerned, but upon quantitative-factors, then we may experimentally vary the latter, comparing, for example, the effect of weak auditory and strong optical stimuli. If quantitative factors govern the response, then we should obtain a greater response to strong light than to weak auditory stimuli. Further, if our supposition is true, these two stimuli might be so adjusted as to produce equal reflex responses.

The observations recorded in the present paper were based upon such an hypothesis.

Observations had already been made in the laboratory relating to this problem, but being directed to other purposes, did not provide the facts which were of primary interest to us. Thus, Palladin [4] formed a conditioned reflex by the summation of stimuli (simultaneous thermal —cold—with scratching stimuli). When each component was separately employed it was found that a response equal to that obtained on combination of the two resulted from scratching, while cold alone gave either no response or a minimal one. However, the continued use of cold as a stimulus finally evoked a constant response, but one less than that elicited by scratching. Thus in a complex of qualitatively different stimuli the response depends upon the more potent stimulus. Perlzweig [5] confirmed these observations. We have extended them to include auditory and optical, auditory and thermal combinations. In one dog we formed a conditioned reflex to a faint sound (Galton's whistle) applied simultaneously with a strong light (400 candle-power), the sound of the whistle being muffled by placing it in a large bottle so that it was scarcely audible to the human ear at 40 cm. distance from

the bottle. In another dog a reflex was established to an electric bell and a metronome 160, and a negative conditioned reflex to the metronome 90, and then a reflex to the tone "Do" of a pitch-pipe. All these reflexes were built upon the unconditioned food reflex (feeding with a moist meat-bread powder).

Observation 1.—Using the dog "Rogdie," the following complex conditioned stimulus was employed: thirty flashes per second of a 400 candle-power lamp with a tone of Galton's whistle (1,500 vibrations). A reflex was established after the second trial and rapidly became stable, that is, it gave constant manometer readings. After the thirteenth combination of this stimulus with feeding, the light stimulus alone unaccompanied by feeding was tried. It gave the same response as the complex light-sound stimulus. On the following day, the complex stimulus having retained its potency, the tone stimulus alone was employed. It gave a secretion of six divisions on the manometer, that is, a response 12·5 per cent. of the response to the light-sound complex.

These observations are recorded in the following table:—

TABLE I.—DOG "ROGDIE."

Time	Number of trials	Conditioned stimulus	Duration of stimulus	Latency of response	Manometer reading	With feeding = + Without ,, = −
(Oct. 22, 1925)						
4.33	35th	Bell	30 sec.	16 sec.	28	+
4.40	43rd	Metronome 160	30 ,,	5 ,,	58	+
4.50	13th	Light and tone	30 ,,	4 ,,	47	+
5.02	44th	Metronome 160	30 ,,	4 ,,	48	+
5.10	1st	Light alone ..	30 ,,	3 ,,	48	−
5.13	36th	Bell	30 ,,	2 ,,	87	+
5.17	45th	Metronome 160	30 ,,	5 ,,	54	+
(Oct. 23, 1925)						
3.40	46th	Metronome 160	30 ,,	2 ,,	22	+
3.46	14th	Light and tone	30 ,,	4 ,,	48	+
3.56	47th	Metronome 160	30 ,,	5 ,,	58	+
4.04	1st	Tone alone ..	30 ,,	13 ,,	6	−
4.07	37th	Bell	30 ,,	1 ,,	67	+
4.15	20th	Metronome 90	30 ,,	28 ,,	1	−
4.19	48th	Metronome 160	30 ,,	10 ,,	28	+
4.25	49th	Metronome 160	30 ,,	7 ,,	50	+

The strength of the tone was then slightly increased and the new complex stimulus tried fifteen times, and then the tone alone unnaccompanied by feeding. The complex gave a manometer reading of 50, the tone alone one of 8 (16 per cent.).

The tone was again increased so that it became clearly audible

outside the dog's cell through the open door in the next room. The strengthened complex was repeated eighteen times, and then the two components tried separately, this time accompanied by feeding.

TABLE II.—DOG "ROGDIE."

Time	Number of trials	Conditioned stimulus	Duration of stimulus	Latency of response	Manometer reading	With feeding = + Without ,, = -
(Nov. 5, 1925)						
4.02	61st	Metronome 160	30 sec.	5 sec.	77	+
4.10	30th	Light and tone	30 ,,	6 ,,	50	+
4.23	62nd	Metronome 160	30 ,,	7 ,,	47	+
4.30	2nd	Tone alone ..	30 ,,	8 ,,	8	−
4.35	24th	Metronome 90	30 ,,	8 ,,	2	−
4.36	44th	Bell	30 ,,	2 ,,	86	+

TABLE III.

Time	Number of trials	Conditioned stimulus	Duration of stimulus	Latency of response	Manometer reading	With feeding = + Without ,, = -
(Nov. 20, 1925)						
9.20	80th	Metronome 160	30 sec.	3 sec.	52	+
9.25	61st	Bell	30 ,,	2 ,,	83	+
9.33	49th	Light and tone	30 ,,	3 ,,	54	+
9.41	62nd	Bell	30 ,,	2 ,,	80	+
9.47	1st	Tone alone ..	30 ,,	3 ,,	12	−
9.57	37th	Metronome 90	30 ,,	3 ,,	18	−
10.02	81st	Metronome 160	30 ,,	2 ,,	75	+

TABLE IV.

Time	Number of trials	Conditioned stimulus	Duration of stimulus	Latency of response	Manometer reading	With feeding = + Without ,, = -
(Nov. 23, 1925)						
10.00	63rd	Bell	30 sec.	4 sec.	56	+
10.06	82nd	Metronome 160	30 ,,	2 ,,	62	+
10.14	2nd	Tone alone ..	30 ,,	7 ,,	13	+
10.19	64th	Bell	30 ,,	5 ,,	55	+
10.26	3rd	Light alone ..	30 ,,	4 ,,	35	+
10.30	38th	Metronome 90	30 ,,	—	—	−
10.38	3rd	Tone alone ..	30 ,,	6 ,,	20	+
10.43	83rd	Metronome 160	30 ,,	2 ,,	60	+
10.48	4th	Tone alone ..	30 ,,	3 ,,	20	+
(Nov. 28, 1925)						
10.10	87th	Metronome 160	30 ,,	3 ,,	60	+
10.18	69th	Bell	30 ,,	4 ,,	62	+
10.24	9th	Tone alone ..	30 ,,	5 ,,	26	+
10.30	7th	Light alone ..	30 ,,	5 ,,	42	+
10.40	42nd	Metronome 90	30 ,,	—	—	−
10.48	70th	Bell	30 ,,	6 ,,	42	+
(Dec. 8, 1925)						
10.15	96th	Metronome 160	30 ,,	3 ,,	58	+
10.20	11th	Light alone ..	30 ,,	3 ,,	62	+
10.28	77th	Bell	30 ,,	4 ,,	78	+
10.35	16th	Tone	30 ,,	3 ,,	60	+
10.42	48th	Metronome 90	30 ,,	4 ,,	14	−
10.52	97th	Metronome 160	30 ,,	3 ,,	70	+
11.00	78th	Bell	30 ,,	3 ,,	80	+
11.07	13th	Light alone ..	30 ,,	2 ,,	53	+

In Tables III and IV is seen that when the light and tone stimuli are separately employed, in spite of the increase in strength of the latter, at first the predominant effect was obtained from the light, the tone producing a very small increase in response. Thus, in the first experiment the light alone gave a manometer reading of 25, that is, 71 per cent. of the response to the complex stimulus on the same day of observation. The tone gave a reading of 12, or 22 per cent., of the response to the combined stimuli.

On the basis of the foregoing experiments we may conclude that both light (400 candle-power lamp) and cold (0° C.) are more potent stimuli than very faint sounds. Thus, auditory stimuli are not essentially and qualitatively prepotent. The larger reflex secretory effect obtained on such auditory stimuli as the metronome and the bell depend solely upon their relatively greater strength than light and thermal stimuli. Rikman found the same to be true of tactile stimuli.

Further, our experiments showed that the effect of a stimulus is not entirely dependent upon its quality, that is, upon whether it affects cutaneous, auditory or optical analysers. Cold, the weakest of all stimuli, was combined with a very faint sound (vibration of the metallic disc of a telephone receiver) which could be increased to threshold value, and since thermal stimuli are prone to induce a state of drowsiness in the animal, the complex was employed for a short time only (ten to fifteen seconds). The results were comparable with those obtained by a light-tone complex.

The faint telephone vibration is a weaker stimulus than the application of cold (0° C.). In the first observations cold gave a manometer reading of 21, telephone of 7 only. After the separate application of each stimulus, the relative strength of the response to the telephone alone increased, but remained less than that to the cold stimulus.

In the experiment shown for March 15 (Table V), cold gave a reflex corresponding to 34 divisions of our scale, and the telephone a reflex corresponding to 22, and this relation between the two persisted until the end of our work.

We should like to call attention to the following fact in the mechanism of the reflex to complex stimuli. When we tried for a long time separately the light and the tone, the effect of the tone was seen gradually to increase, until finally the tone began to give almost the same effect as the light.

TABLE V.

Time	Number of trials	Conditioned stimulus (c.s.)	Duration of action of c.s.	Latent period of conditioned salivary secretion	Manometer reading	With feeding = + Without ,, = −
(Feb. 10, 1926)						
3.44	5th	Do (pitch-pipe)	30 sec.	4 sec.	76	+
3.24	24th	Cold-telephone	15 ,,	8 ,,	12	+
3.31	6th	Do (pitch-pipe)	30 ,,	5 ,,	50	+
3.36	25th	Cold-telephone	30 ,,	6 ,,	23	+
3.42	69th	Metronome 90	30 ,,	7 ,,	8	−
3.48	55th	Bell	30 ,,	5 ,,	46	+
3.53	26th	Cold-telephone	30 ,,	7 ,,	34	+
(Feb. 18, 1926)						
4.30	35th	Cold telephone	10 ,,	6 ,,	2	+
4.40	57th	Bell	30 ,,	4 ,,	57	+
4.47	36th	Cold-telephone	30 ,,	7 ,,	22	+
4.52	72nd	Metronome 90	30 ,,	20 ,,	3	−
5.02	120th	Metronome 160	30 ,,	8 ,,	52	+
5.07	8th	Do (pitch-pipe)	30 ,,	6 ,,	48	+
(Feb. 19, 1926)						
4.44	58th	Bell	30 ,,	5 ,,	42	+
4.48	37th	Cold-telephone	30 ,,	—	—	+
5.05	121st	Metronome 160	30 ,,	5 ,,	60	+
5.10	38th	Cold-telephone	30 ,,	8 ,,	3	+
5.18	1st	Cold (alone) ..	30 ,,	7 ,,	21	+
5.29	1st	Telephone(alone)	30 ,,	9 ,,	7	+
(Feb. 26, 1926)						
4.40	45th	Cold-telephone	15 ,,	—	—	+
4.48	125th	Metronome 160	30 ,,	10 ,,	37	+
4.53	4th	Cold (alone) ..	30 ,,	7 ,,	22	+
4.58	75th	Metronome 90	30 ,,	6 ,,	6	−
5.04	11th	Do (pitch-pipe)	30 ,,	4 ,,	40	+
5.10	46th	Cold-telephone	15 ,,	8 ,,	2	+
(Feb. 27, 1926)						
4.34	47th	Cold-telephone	15 ,,	8 ,,	6	+
4.42	12th	Do (pitch-pipe)	30 ,,	6 ,,	50	+
4.50	4th	Telephone(alone)	30 ,,	7 ,,	11	+
4.59	29th	Light (alone) ..	30 ,,	6 ,,	42	+
(Mar. 15, 1926)						
4.47	17th	Do (pitch-pipe)	30 ,,	6 ,,	54	+
4.53	134th	Metronome 160	30 ,,	3 ,,	78	+
5.00	11th	Cold (alone) ..	30 ,,	8 ,,	34	+
5.08	135th	Metronome 160	30 ,,	5 ,,	63	+
5.14	12th	Telephone(alone)	30 ,,	4 ,,	22	+

From these observations we may conclude that in the complex stimulus the weaker component cannot exert its own full effect because it is in a state of partial suppression by the stronger component. Such an inhibition of the weaker by the stronger component is in all probability a general rule when two or more stimuli are combined in a complex. There is, as a consequence, a constant struggle or conflict between different points of excitation in the cerebral cortex.

There may be not only a suppression of the weaker component, but also a mutual influence of one on the other, the weaker stimulus may

in some measure diminish the influence of the stronger. Observations made by Yakovleva [7] and by ourselves incline us to this view. We found that when the strength of a tone was greatly increased the response to a complex stimulus of which it is a component becomes for the next few days irregular and smaller. Evidently new relations are set up between the components, and a certain length of time is necessary to establish a new equilibrium between light and tone.

These experiments do not afford a conclusive answer to the question of the specificity of function of different parts of the brain, but they suggest that all parts of the cerebral cortex function in the same way and are subject to the same factors. The possibility of differences of functional activity is not excluded, but if such differences exist they are of a quantitative order only. In reality the determining factor is the energy which acts upon the nervous elements of the cortex. Further and more exact observations are necessary for a final decision of the question. For example, we must have exact quantitative estimations of the energy which acts upon the various peripheral receptors on stimulation, the extent to which this energy is transformed into the nervous impulse, and its strength when it reaches the cerebral cortex. If it could be demonstrated that there is an exact correspondence between the size of the reaction and the intensity of the nervous impulse which reaches the cortex, we might conclude that cerebral activity is conditioned entirely by external factors.

Summary.

(1) Separate employment of the components of a complex conditioned stimulus is a reliable method of determining their relative strengths.

(2) In a complex of two stimuli, the main effect is produced by the stronger stimulus, and this may even inhibit the weaker component.

(3) A strong light (400 candle-power lamp) and cold (0° C.) are more potent stimuli than a very faint sound.

(4) The size of the conditioned reflex reaction depends upon the strength of the stimulus, that is, upon the energy transmitted to the cerebral cortex.

(5) The comparative effects of different stimuli depend upon the intensities of these stimuli, regardless of the analyser to which they belong.

(6) Our observations incline us to the view that the various regions

of the cerebral cortex function, in the main, identically and such differences as may exist from region to region are of a quantitative order only.[1]

REFERENCES.

[1] Rikman. Unpublished work.
[2] Kasherinova, M. N. "Dissertation," St. Petersburg, 1908 (Russian).
[3] Orbeli, L. A. "Dissertation," St. Petersburg, 1908 (Russian).
[4] Palladin, A. W. "Trudi Obshestva Rooskich Vrachi," 1906, **77**.
[5] Perlzweig, I. A. "Dissertation," St. Petersburg, 1907.
[6] Tichimirov, N. P. "Trudi Obshestva Rooskich Vrachi," 1910 (Russian), **77**.
[7] Yakovleva, V. V. *Russian Journ. of Physiology*,1926, **9**, 139.
[8] Zelony, G. P. "Dissertation," St. Petersburg, 1907 (Russian).
[9] *Idem*. "Trudi Obshestva Rooskich Vrachi, 1910, **77** (Russian).

[1] We desire to thank Dr. F. M. R. Walshe for certain suggestions as to the phraseology in this article.

THE ENDOCRINES IN EPILEPSY: A HISTOLOGICAL STUDY.

BY H. I. SCHOU,

Hospital for Epilepsy and Mental Diseases, Dianalund, Denmark,

AND

WM. SUSMAN,

Department of Pathology, Manchester University.

In the study of the pathogenesis of epilepsy, recent investigators have turned more and more away from the endocrines as a possible factor in the disease. Clinical observations, however, point in the direction of an intimate association of epilepsy with endocrine derangement. For example, the incidence of initial attacks at puberty (*circa* 40 per cent.), the relationship of fits to menstruation and pregnancy, the association with parathyreopriva and diabetes mellitus, &c.—all these are suggestive. Clinical symptoms suggesting pluriglandular insufficiency are also associated rather frequently with epilepsy, for example, abnormal obesity, hirsuties, abnormal pigmentation, increased nervous irritability (Chvostek's and Erb's "phenomena"), lack of calcium in the blood and spinal fluid, &c. Though these do not prove a definite causal relationship, they do indicate the necessity for a careful investigation both in the laboratory and at the bedside.

It is curious that in the past the endocrine glands have been examined in very few cases, and by only a small number of investigators. Claude and Schmiergeld [1] in 1907 and 1909 published their results of an investigation on the ductless glands of seventeen cases of epilepsy (all females). They found very extensive and intensive alterations in almost all the glands, especially in the thyroid, parathyroids, pituitary, and adrenals, and to a lesser degree in the ovaries and pancreas. The lesions included sclerosis, alterations and degeneration of the parenchymal cells, and less frequently hypertrophy and vascular disturbances. "Lesions in the endocrine glands of epileptics are of frequent occurrence, but they vary in character and distribution. However, our results demand further study." Such is the conclusion of these workers. Volland [4] very frequently found masses of lipoid within the cell protoplasm of the liver, kidneys, spleen and pancreas in those that had died during *status*

epilepticus; he believed that these alterations also follow epileptic seizures. In the pituitary the results were always negative. Erdheim [2] in two cases of status epilepticus found the parathyroids quite normal. The communication of Esquirol [3] is of interest. In seven out of twenty cases he found the pituitary enlarged, and in ten cases there was a solid compact yellow mass within the gland.

The evident lack of uniformity in the results obtained by the above investigators in itself demands a further inquiry.

The results of our investigation of the following small series of cases are not in any respect indicative of a solution to these very difficult problems. On the contrary this is but a beginning. We only intend to draw attention to the facts that there are often alterations in the endocrines of epileptics. If these can be confirmed in a larger series of cases—as we hope to do at a later date—then only will it be opportune to discuss the significance in these findings in so far as they may influence the clinical and therapeutic aspects.

Various endocrines and the genital glands of six cases and the liver from one case of epilepsy were available for examination. The tissues were fixed in Helly's fluid. Sections were stained by hæmalum and eosin, and by acid fuchsin and methyl green.

The following represents a summary of the microscopic examination of the various organs, and a brief history of each case.

Case 1.—E. J. No. 2870. Female, aged 32.

History.—No hereditary predisposition. Duration seven years. Initial attack during pregnancy. A few major and some minor attacks.

Cause of death: Prostatio epileptica[1] and pneumonia.

Microscopic Examination.

Ovaries.—Numerous purplish areas are scattered over the sections. They are associated chiefly with the adventitia of large and medium sized arteries. Occasionally this necrotic process involves portions of the medial and subintimal coats. Many of the involved vessels contain inflammatory products, as serum, inflammatory cells, &c., in their perivascular channels.

Oviducts.—In the surrounding tissue there are numerous necrotic areas associated with the perivascular channels of the arteries.

Adrenals.—Numerous small groups of cortical cells are disintegrating and an early fibrosis is in progress in such areas. There are small purple intra- and extra-cellular masses of necrotic material in the cortex. In the medulla, the

[1] By prostatio epileptica we mean a slow decrease of the vitality of the epileptic accompanied by fever and terminating in death by paralysis cordis. In epilepsy the death-rate of this group is a characteristic feature.

cells are widely separated by dense fibrous tissue. Many possess very large nuclei. Of the latter, a large proportion are in achromatosis, or the nucleus is shrivelled and irregular. Necrosis has involved the perivascular regions of the large adrenal arteries.

Thyroid.—Cystic involution. Perivascular and perivesicular necrosis is not uncommon.

Pancreas.—The acini are in a pronounced state of atrophy. Interacinar fibrosis and acinar disorganization are common features. In this organ necrosis of the variety already described has attacked the perivascular and periductal zones. The islets are extremely hypertrophied and abundant. There are several pseudo-islets.

Parathyroids.—The glandules are enlarged. There is an appreciable amount of fat in the fibrous tissue stroma. Again, necrosis is present in the perivascular region of the large arteries. The oxyphilic cells are numerous and probably predominate. Some are very large and extremely granular, while the majority are only slightly larger than the cells with the clear non-staining cytoplasm.

Replacement fibrosis is in progress in several fairly large areas where degeneration had occurred.

Case 2.—T. K. J. No. 955. Female, aged 40.

History.—No hereditary predisposition. First attack when 9 years of age, after scarlatina. Five minor attacks every month. Occasionally forty severe and minor attacks in one month.

Cause of death.—Acute peritonitis and abscess.

Microscopic Examination.

Ovaries.—Unilocular cysts. Small areas of necrosis, as already described, occur frequently in both the ovarian substance and in the perivascular channels of the arteries.

Pituitary.—The pars glandularis is enlarged to about twice the usual size. Many chromaffin cells contain very enlarged nuclei and some exhibit achromatosis. There are several calcareous deposits in the capsule of the gland.

Thyroid.—There is a very pronounced fibrosis. The vesicles are filled with desquamated epithelium and inflammatory cells. Several large degenerated areas have been invaded by small round cells and fibrosis. Purplish staining areas of necrosis of perivascular and perivesicular distribution occur frequently.

Parathyroids.—Enlarged. Pronounced fatty infiltration. Oxyphilic cells are abundant but do not predominate; numerous small groups of cells have disintegrated, but such areas show nothing distinctive.

Case 3.—K. K. No. 1367. Male, aged 31.

History.—No hereditary predisposition. Duration thirty-one years. Five severe attacks every month.

Cause of death.—Prostatio epileptica and broncho-pneumonia.

Microscopic Examination.

Testicle.—Fibrous thickening of the tunica vaginalis is pronounced. Small foci of necrosis are frequently seen, particularly in association with the perivascular channels of the larger arteries. There are small nodules of small round cells, some are perivascular in distribution. This suggests syphilis. Spermatogenesis was normal.

Pancreas.—The acini generally are disorganized and the acinar cells atrophic. There is some interacinar fibrosis. The islets are extremely enlarged, and their vessel walls exhibit fibrous thickening. A small number of islet cells are globulated. Mitosis is not uncommon. Pseudo-islets are present. Perivascular necrosis is seen occasionally about both the acinar and islet vessels.

Thyroid.—Proliferation and desquamation of vesicular epithelium, colloid in the interstitial tissue, and interstitial thyroid cells are abundant, while fibrosis is very pronounced. Perivascular necrosis is again evident.

Parathyroids.—Enlarged. Fatty infiltration is very pronounced. Occasional groups of cells have disintegrated, but there is no evidence of inflammation.

Oxyphilic cells are very numerous, but do not predominate. On examination, by an oil immersion lens, large rod-shaped granules which stain red with acid fuchsin lie embedded in the cytoplasm of the cells of colourless cytoplasm.

Case 4.—C. C. No. 2037. Female, aged 22.

History.—No hereditary predisposition. Duration, fourteen years. Every month five minor and several severe attacks. Status epilepticus once.

Cause of death.—Lobar pneumonia.

Microscopic Examination.

Ovaries.—Unilocular cysts; areas of perivascular necrosis fairly numerous.

Oviducts.—Normal except for perivascular necrosis.

Thyroid.—Vesicles enlarged but not cystic. Interstitial cells abundant. Perivascular necrosis common. Proliferation and desquamation of vesicular epithelium as in acute diseases.

Adrenals.—In the medulla there are large, well-encapsulated calcifical areas. About the larger arteries perivascular necrosis is common.

Parathyroids.—Enlarged. Oxyphilic cells predominate. Several large areas of degeneration are present, some are invaded by hæmorrhage, while others show varying degrees of fibrosis.

Case 5.—L. A. No. 1261. Female, aged 26.

History.—No hereditary predisposition. Duration thirteen years. Ten severe and a few minor attacks every month.

Cause of death.—Acute pericarditis.

Microscopic Examination.

Ovaries.—Unilocular cysts. Several foci of chronic inflammation. Necrosis in perivascular channels and within ovarian substance.

Pancreas.—Perivascular necrosis is pronounced, especially about the larger

vessels. Disorganization of acini and interacinar fibrosis have occurred. The islets are extremely enlarged.

Pituitary.—Many small groups of cells are necrosed. Large dark nucleated chromophobe and chromophile cells are frequently seen. Perivascular necrosis is again present.

Case 6.—Male, aged 35. Mild epileptic not under institutional care.

Cause of death.—Contusion of the brain as result of a street accident.

Microscopic Examination.

Thyroid.—Nothing particularly abnormal.

Pituitary.—Pars glandularis appreciably enlarged.

Liver.—There are many small nodules of fibrous tissue containing small round cells, as well as numerous acute and subacute foci, scattered over the section. A considerable amount of cellular disintegration has occurred as a result of a generalized passive congestion in the liver.

Parathyroids.—The cells are largely of the oxyphilic type, and there are many of the transitional variety. A non-inflammatory cellular disintegration has occurred and has been followed by fibrous replacement. Mitosis is not infrequent. Two large areas suggest that hyperplasia had taken place.

Discussion.

Unfortunately all the endocrines in all cases were not available for examination. Even under these circumstances one can readily realize that there were constant changes in several organs.

The lesions in the genital glands were not distinctive.

When the patient had died from an acute infectious disease the thyroid showed the usual acute reaction. Otherwise there was a distinct lesion, and active degeneration was present in one gland out of a total of four examined. In one other there was a pronounced fibrosis.

In one or two pairs of adrenals examined, many medullary cells were enlarged and showed degeneration; there was an associated fibrosis. The whole picture indicates a slow chronic inflammation.

The pars glandularis of the pituitary glands (four examined) were all enlarged and usually to a very pronounced degree.

A comparison between the lesions in the adrenal medulla and those in the anterior pituitary shows a certain similarity. In both the destructive agent has a preference for the chromophile cells, producing a similar type of large cell with a very large nucleus which frequently showed signs of degeneration. In the adrenal the process was of a longer standing, since dense fibrous tissue had appeared.

The pancreatic lesions display a very striking uniformity. In all three available there were acinar disorganization, interacinar fibrosis, and extremely enlarged islets. Mitosis in islet cells was common. There are therefore, in the epileptic pancreas, if these be taken as true examples, many features in common with the diabetic pancreas. But one very outstanding and significant divergence from this comparison exists. In both acinar disorganization is a feature; although in the epileptics of this series it is constant, in diabetics it is found only in a large proportion. The same applies to interacinar fibrosis. But with hypertrophied islets the divergence arises. In the diabetics hypertrophied islets are a relatively common feature, but they are not so numerous and they accompany islet degeneration. The epileptic pancreas has only a negligible number of islets showing any recognizable signs of degeneration; the hypertrophied islets are in a real sense abundant, and mitosis in islet cells is frequently seen. On the whole, this would indicate functional strain on the islets, even though the actual degenerative lesions of diabetes are absent.

There still remain the parathyroids to be considered. The external parathyroids of each case alone were examined. All were enlarged, showed abundant oxyphilic cells, and a few contained areas of degeneration.

In view of the fact that there was neither congestion nor cysts to account for the enlargement, hypertrophy must have existed. This gains further support from the state and abundance of oxyphilic cells.

Unpublished experiments by one of the writers (W. S.) showed that the parathyroid under strain becomes enlarged, the oxyphilic cells abundant and very granular, and the colourless cells are finely globulated. Further, MacCallum, in two cases, found that hyperactivity of the parathyroids is associated with increased granularity of the oxyphilic cells. Therefore the external glandules of all the cases of this series gave abundant evidence of increased activity. The degenerative areas support this view, in that inflammation is lacking, and the appearance is rather one of disintegration following on excessive functional strain.

In one case only was the liver examined. There small, widely scattered inflammatory foci in various stages were present. These may correspond very well with the periodic attacks of epilepsy.

All organs examined in the first five cases gave ample evidence of perivascular necrosis. The sixth, a mild case, showed no such lesion.

That there are significant lesions in these cases is obvious. They

can be divided into several groups. Firstly, hypertrophy was a feature of the parathyroids, the pituitaries and the islets of Langerhans. Secondly, the liver, the islets of Langerhans, the pituitary and adrenal are concerned with the carbohydrate metabolism. These all showed lesions. This is also true of the acinar tissue of the pancreas. Thirdly, the pathological agent has a selective action on chromophile cells, as seen in the adrenals and pituitaries. Fourthly, a toxic necrosis is present in the perivascular channels of all the organs examined, if the case has been a severe one.

This can be considered only as suggestive. Many further problems arise which require further study.

At this point it is necessary to state only that:—

(1) According to the results of investigation which have been recorded, and according to our personal experience, the appearance of normal endocrine glands is quite definitely established.

(2) The lesions described in the epileptic cases of this series are without any doubt deviations from the normal.

(3) A corresponding investigation of endocrine glands from patients that had died from the common prostrating and infectious diseases did not show such lesions.

We do not wish to suggest conclusions of a clinical or therapeutic nature, as this is a preliminary study. We also understand clearly the desirability of examining glands from early cases of epilepsy, and glands from epileptics who died suddenly without long prostrating bodily disease. This we hope to accomplish.

To Dr. Duguid we are indebted for the sections of Case 6, for the use of which we express our thanks.

REFERENCES.

[1] Claude, H., and Schmiergeld, A. "Les glandes des sécrétions internes chez les épileptiques," *L'Encéphale*, January 10, 1909, 1.

[2] Erdheim. Cit. a. Falta, *Die Erkrankungen der Blutdrüsen*, p. 167.

[3] Esquirol. "Malades Mentales," **1**, 310.

[4] Volland. "Organuntersuchungen bei Epilepsie," *Zeit. f. d. ges. Neur. u. Psych.*, 1910, **3**.

THE CEREBELLAR TERMINATIONS OF THE SPINO-CEREBELLAR FIBRES OF THE LOWER LUMBAR AND SACRAL SEGMENTS OF THE CAT.

BY GILBERT M. BECK.

(Henry J. Phipps Psychiatric Clinic, Johns Hopkins Hospital, Baltimore.)

I.—Bibliographical Survey.

As early as 1844, Fouville [11] found that in the lateral border of the spinal cord was a tract myelinated before any of the contiguous fibre groups. Türck [49] discovered later that in certain tracts of the spinal cord the nerve fibres undergo secondary degeneration when they are severed from their nerve cells. He found an ascending degeneration in the lateral columns which he traced into the homolateral restiform body and from thence to the cerebellum. The ascending nature of this tract was also observed by Bastian [2] in the post-mortem examination of a case of paraplegia, and then by Bouchard [5] in a case of transverse myelitis and one of carcinoma of the vertebral column.

Not until thirty years after the work of Fouville did Flechsig confirm the ascending nature of this lateral tract, and find "selective" myelinization of it occurring simultaneously with that in the cerebellum. This worker also described the topographical positions of this spino-cerebellar tract; and in so doing almost succeeded in working out the dual composition of the laterally placed spino-cerebellar fibre complex, for he described two rather distinct parts of what he thought to be but one tract, in the cervical cord. And to Flechsig, we also owe the first intimation of a connection between Clarke's column cells and the cerebellum, for he actually traced myelinated fibres to the superior vermis.

But it remained for Gowers [15] to describe the ventral portion of this band as a distinct entity from the dorsal, exclusively cerebellar, tract. This work was made possible through the post-mortem examination of a human cord with a traumatic lesion of the upper lumbar enlargement. He thought the tract extended in cross-sections of the spinal cord as far as the anterior fissure ventrally, and perhaps terminated superiorly in the lateral nucleus of the reticulum.

From that time up to a comparatively recent date, the exact course, and more particularly the origin and termination of these fasciculi, have been the subject of much dispute.

There had appeared in conjunction with the experimental researches of Bing and Salisbury, MacNalty and Sir Victor Horsley, two most excellent reviews of the literature of the lateral tracts; Robert Bing's, a most exhaustive study with an extraordinarily complete bibliography, while that published two years later by MacNalty and Horsley was a uniquely brief tabulated digest of the researches done on these tracts up to the year 1909.

It was thought that a revised tabulation of the known data on the spino-cerebellar fasciculi would be useful. My aim in the revision is, firstly, to bring the literature if possible up to date; and secondly, to group the experimental results into a more comprehensibly useful form.

The story of the unravelling of the skein of evidence that has led to our present-day knowledge of these tracts would be most fascinating. But this type of chronological survey has appeared in the many monographs of successive investigators, as fragment upon fragment was added to make up our present-day store of facts. Such a survey may be found in the works of Mott, Patrick, Bing, Ingvar, &c.

A tabulation of the known facts on the spino-cerebellar tracts is, however, provided. It will be observed that there are a number of unfilled spaces; these are meant to indicate that I have been unable to find any mention of this particular fact in the work of the investigator referred to. The tabulation, therefore, has a twofold advantage in giving to the reader, in a short, concise way, the positive findings of the successive experimenters, as well as the essential data not recorded by them.

II.—Purpose of the Investigation.

This investigation was originally instigated to observe the physiological manifestations after single and double, homolateral and contralateral sections of the spino-cerebellar tracts. After a brief study of the literature it seemed imperative to solve first some of the still confusing facts concerning the morphology of the spino-cerebellar tracts.

Unfortunately I did not attempt to limit the operative section to one spino-cerebellar tract. There is, therefore, no experiment in which either a degenerated ventral spino-cerebellar tract or a dorsal spino-cerebellar

Author	Type of investigation	Origin of d. s.-c.	Origin of v. s.-c. tract	Termination of d. s.-c. tract	Termination of v. s.-c. tract	Crossing of d. s.-c. in cord	Crossing of v. s.-c. in cord
Flechsig (1876)	Myelinization of fœtal cords	Clarke's cells	—	Superior vermis.. ..	—	—	—
Gowers (1880)	Case of paraplegia	Posterior column cells	Anterior horn cells	Superior vermis.. ..	Lateral nucleus	—	Partial
Löwenthal (1883) . ..	Experimental lesion in dog	—	Anterior horn cells	Superior vermis.. ..	Cerebellum (?)	—	—
Tooth (1887)	Experimental degeneration of medulla of monkey	Clarke's column cells	Clarke's column and anterior horn cells	Cerebellum	Cerebellum	—	No
Edinger (1889)	Anatomical work on cords of fish, reptiles, amphibia; studies in myelinization	Clarke's column cells	Posterior horn cells	Superior vermis.. ..	Superior vermis (ventral portion)	Total	Majority
Auerbach (1890) (1904) ..	Experimental degeneration	Clarke's column cells	—	Superior vermis (dorsal portion)	Superior vermis (ventral portion)	No	Partial
Becterew (1890)	Myelinization method	Clarke's column cells	Cells between the dorsal and ventral horns	Superior vermis (anterior portion)	Superior vermis.. ..	No (?)	No (?)
Mott (1892) (1895) ..	Degeneration in monkey	Clarke's column cells	Lateral horn cells	Superior vermis (ventral portion)	Superior vermis (anterior portion)	Partial	Partial
Testut (1893)	Anatomical evidence	Clarke's column cells	Clarke's column cells	Superior vermis.. ..	Superior vermis; nucleus of lateral funiculus	Total	No
Grünbaum (1894)	Degenerative evidence (experimental)	—	Contra-lateral dorsal horn cells	Superior vermis (caudal portion)	Superior vermis (?)	—	Complete
Pellizi (1895)	Experimental degeneration	—	Clarke's column cells or their homologues	Superior vermis (anterior portion)	Superior vermis (antero-inferior portion)	Total	Partial
Patrick (1896)	Experimental degeneration in cat	—	Posterior horn cells	Superior vermis; inferior vermis	Superior vermis (ventral and more distal portions)	—	—
Hoche (1896)	Human cases	—	Posterior horn cells	Superior vermis.. ..	Superior vermis.. ..	—	—
Rossolimo (1898)	Human case	—	—	Superior vermis.. ..	Substantia nigra; colliculus inferior; globus pallidus	—	—

Bruce, A. (1899)	Human case of tumour—degenerative evidence	—	—	Superior vermis; inferior vermis	Superior vermis; nucleus of lateral funiculus	Few	No
Schäfer (1899) and A. N. Bruce (1906)	Chromolytic evidence; degenerative evidence	Clarke's column cells (high)	Clarke's column cells (low)	Superior vermis; inferior vermis	Superior vermis; inferior vermis	Partial	Partial
Kohnstamm (1900) ..	Experimental degeneration in dogs	—	Ventral horn cells; middlecells; cells at base of posterior horn	—	Superior vermis.. ..	—	—
Van Gehuchten (1900) ..	Degenerative evidence	Clarke's column cells	Cells of posterior column	Superior vermis (posterior portion)	Superior vermis (anterior portion	Partial	Complete
Collier and Buzzard (1903)	Clinical cases; degenerative evidence	—	—	Superior vermis; inferior vermis; dentate nucleus; lateral lobe of hemispheres	Superior vermis; Deiters' nucleus; Bechterew's nucleus; flocculus	—	—
Lewandowsky (1904) ..	Animal experimentation	Clarke's column cells	Clarke's column cells	Superior vermis; nucleus of lateral funiculus and its accessory nucleus	Inferior vermis; nucleus of lateral funiculus and its accessory nucleus	Small number of fibres	Small number of fibres
Marburg (1904)	Human cases of cord compression	Clarke's column cells	Clarke's column cells	Anterior vermis	Anterior vermis	—	—
Bing (1907)	Experimental degeneration in the dog	Clarke's column cells	Cells of lateral portion of anterior horn	Superior vermis(anterior-superior portion)	Superior vermis (antero-inferior portion)	Majority	Perhaps total
MacNalty and Horsley (1909)	Experimental degeneration in the cat, dog and monkey	—	—	Superior vermis (lobulus centralis, culmen); inferior vermis (declive and pyramis)	Superior vermis (lobulus centralis, culmen); inferior vermis (declive)	1 in 4	1 in 2
André-Thomas (1897) (1912)	Degeneration in human case	Clarke's column cells	Cells at base of anterior horn	Superior vermis (anterior portion)	Anterior vermis (perhaps lateral nucleus, nucleus fastigii)	Majority	Wholly (?)
Obersteiner (1914) ..	Human cases of disease of spinal cord	Clarke's column cells	Cells of middle of central grey; Clarke's column cells	Vermis	Superior vermis (anterior portion); grey matter cervical cord	—	Partial
Horrax (1915)	Animal experimental degeneration	—	—	Inferior vermis; medial portion of lateral hemisphere	Superior vermis.. ..	Majority	Majority
Ingvar (1918)	Experimental degeneration in the dog and cat	—	—	Superior vermis (lobulus centralis, culmen); inferior vermis (declive, uvula, pyramis)	Superior vermis (lobulus centralis, culmen)	—	—

tract appears alone. It is regrettable that this point was not anticipated, for the section of but one tract alone would have given more definite results. As it is, although the terminations of the spino-cerebellar tracts in our sections are very distinct, they are not as unmistakably definite as the presence of a single degenerated tract only could make them.

III.—Method of Investigation.

The work was limited to an investigation of the dorsal and ventral spino-cerebellar tracts in the cat. Forty animals were used. Of this group, ten died of an exceedingly contagious naso-pharyngeal infection; seven died of superficial wound infections which rapidly caused a septicæmia; and four succumbed to undetermined causes.

The cats were placed in deep chloroform narcosis. This was accomplished by means of a pump and mixer from which a definite amount of chloroform and air could be constantly and automatically administered. We used foundling cats of both sexes and many breeds. Large cats were preferred to small ones, and all animals were fully matured. All the surgical procedures were done under aseptic conditions. The bone was removed as gently as possible to avoid profuse bleeding and injury to the cord. Many operations were performed with an almost negligible amount of bleeding.

Both sides of the cord were exposed for a distance of about two or three segments. The section was made without previously opening the dura. A very sharp paracentesis knife was employed to make the slit in the lateral border of the cord. This, also, could be done with a minimal amount of bleeding if one was careful not to pull the dura mater too firmly when entering the cord, and to avoid pushing the knife through the meninges against the bony canal after the substance of the cord was divided.

In all, nineteen animals with single and double sections of the spinal cord survived the requisite Marchi period. As it was not hoped to add any new light on the regional origin of these tracts the sections were not made with that view in mind, but similar lesions were made at various levels. Anatomically this grouping has no significance, but was done rather for the purpose of demonstrating the symptom complex after various single and double contralateral and homolateral sections of the cord.

The operated animals were allowed to live from eight days up to a

period of thirty days. Five animals were sacrificed under fourteen days. Fourteen were allowed to live two weeks after operation; eight of these remained alive after twenty-one days.

It is interesting to note that the specimens of greatest value for anatomical purposes were those obtained respectively 19 days, 13 days, 12 days, 8 and 6 days (cat with double section) after operation. However, well-stained specimens were obtained after 25 days and even after 29 days. The latter sections were from an animal that had two operations, the second one being 14 days before the date of sacrifice. It did seem, in a thirty-day cat, that the substance stained by osmic acid had already undergone some absorption.

On examination of the specimens the problem of explaining the presence of a fine precipitate-like stain that occurred diffusely throughout the white matter of some specimens arose.[1] Are the number of grains directly proportional to the length of time an animal lives past the *optimum* time? Is it due to a post-operative rise of temperature? Or perhaps an improper choice of the embedding process? Each of the foregoing explanations was held by the writer at varying times, all to be discarded at the end of the work. The "dirtiest" of our sections are those from an animal surviving nine days after operation, while a cat with absolutely clean sections has lived nineteen days. It has seemed, nevertheless, that material beyond a two weeks' period was more likely to be mottled with this "precipitate."

At first it seemed that this condition might be due to a post-operative rise in temperature, but as the cord of an animal which had hyperpyrexia for a number of days after the operation was free of "precipitation," while, on the other hand, specimens from animals which, to the best of my knowledge, were temperature-free were filled with this mottled degeneration, it is necessary to assume that temperature, at any rate, is not the sole factor.

Both excellent and extremely poor results were obtained by each method of embedding I employed.

IV.—The Investigation.

For convenience the material may be divided into three groups, namely, the crucial experiments; those which are only confirmatory,

[1] In material containing this "precipitation," one can readily see and map out many bizarre end stations and collateral plexuses which, of course, do not exist. It would seem that the presence of this extraneous matter has, perhaps, been the cause of much of the confusion concerning the morphology of these bundles.

and lastly, those which were useless for my purpose. Of the nineteen experiments, six belong to the first class; nine to the second, in which the gross degenerations are very clear, but accompanied by extraneous staining material so that they were helpful in a confirmatory way only; and to the third class four in which the sections were filled with "precipitate," or the fibre degenerations were so indefinite that they were worthless.

Series of transverse and sagittal sections will be described in detail. The comparison of these different sections furnishes definite data as to the termination and topographical arrangement that would be impossible to discern in sections cut in one plane. A few sections are also described from a horizontally cut brain-stem and cerebellum for the purpose of further clarifying some of the topographical findings.

Cat 2.—Grey and white male. Marchi-Busch staining. Transverse celloidin sections. Nineteenth-day animal.

November 25, 1925: Chloroform anæsthesia. Section of the right first lumbar segment.

December 14: Cat was sacrificed. The brain and cord were removed and placed in 10 per cent. formalin.

December 28: Cord, brain-stem and cerebellum were cut transversely into thirty-five blocks and the thalamus into four blocks, each of 3 mm. in thickness. These blocks were sewed into strips of gauze in serial order with their posterior surfaces upward. They were then immersed in Marchi-Busch fluid (osmic acid 1·0; sodium iodate 3·0; aqua 300·0) and by means of the gauze suspended in the solution. The fluid was kept in a dark cupboard and only removed to shake thoroughly at least once daily, and to add fresh osmic acid every other day. The blocks were removed from the osmic acid at the end of fourteen days, and washed in running water for twenty-four hours. They were then transferred through successive strengths of alcohol and ether, embedded in celloidin, and cut at fifty micra.

This series was almost entirely free of any extraneous stained material. The brain-stem sections were unintentionally cut obliquely so that the left side is slightly cephalad to the right side.

Sacral I.—At the junction of the short, stout posterior horn and the longer anterior horn, there is a small mass of degenerated fibres lying close to and touching the margin of the cord. From here a narrow band of loose fibres extends along the lateral border and along the anterior sulcus to about the ventralmost part of the medial projection of the central grey matter. These fibres represent descending tracts, the most dorsal, no doubt, the tractus cortico-spinalis lateralis.

Lumbar V (fig. 1).—This segment below the lesion shows a clear somewhat triangular space between the posterior horn and the degenerated

pyramidal tract. This space, of course, is not degenerated because it is occupied by the dorsal spino-cerebellar tract. The crossed pyramidal bundle, not very compactly arranged, is placed against the periphery of the lateral column. There is a zone of degenerated fibres along the latero-ventral and ventral

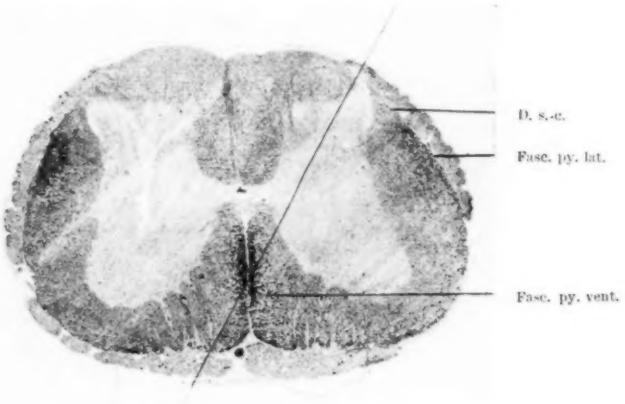


FIG. 1.—First lumbar segment.

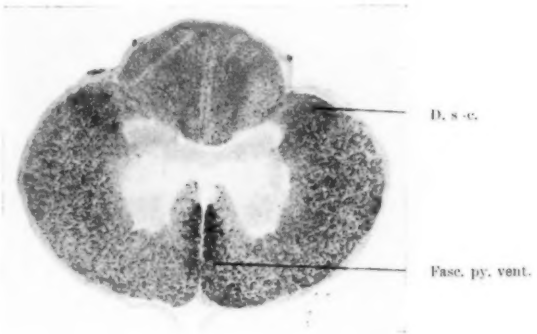


FIG. 2.—Second lumbar segment.

columns that may belong to the tecto-spinal and vestibulo-spinal tracts, at any rate they are descending fibres. The direct pyramidal bundle is thin, dark and rather compact, running along each border of the ventral fissure as far dorsal as the anterior white commissure.

Lumbar II (fig. 2).—The lesion is about at this level; the exact incision, however, could not be demonstrated. The greater part of the lateral and ventral

columns are filled with a homogeneous mass of degenerated fibres, as if this part of the cord were degenerated. There is also some vacuolization. The great bulk of the degeneration in these columns seems to be due to internuncial fibres, for as the cord is ascended they gradually disappear, leaving the degenerated ventral spino-cerebellar and dorsal spino-cerebellar tracts only.

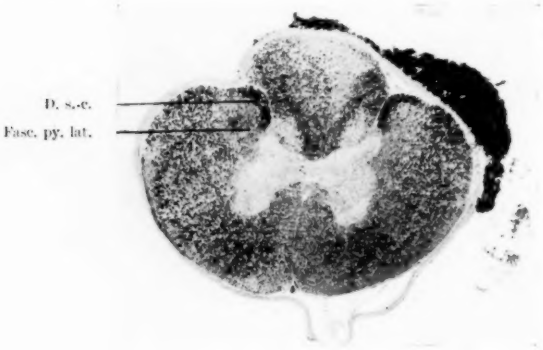


FIG. 3.—First lumbar segment.

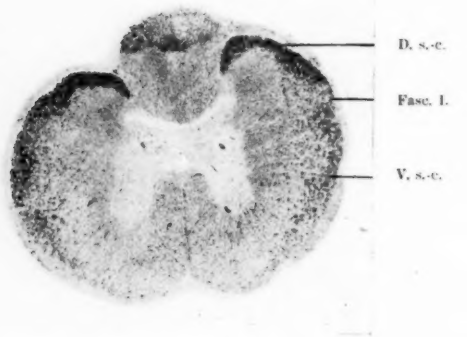


FIG. 4.—Eleventh thoracic segment.

Lumbar I (fig. 3).—This is the first segment above the lesion. Here the dorsal spino-cerebellar tract is degenerated and occupies the position which is evident, although not degenerated, in Lumbar V. The degeneration forms a moderately wide, very concentrated tract capping the cortico-spinal bundle. Because of the many degenerated fibres in the fasciculi proprii, the ventral spino-cerebellar tract does not stand out as a distinct entity.

It is interesting to note that the fibres of the dorsal spino-cerebellar tract seem divided by the jutting out of the lateral pyramidal tract into thick dorsal and ventral groups of fibres with a narrow band between them. The dorsal portion lies along the ventral border of the posterior horn and curls around the periphery of the cord; the ventral part is a thick, somewhat triangular shaped group of concentrated fibres. The exact confines of this dorsal bundle and of the ventral spino-cerebellar tract are not absolutely certain because of the still present degenerated internuncial fibres.

Thoracic XI (fig. 4).—The degenerated fibres in the fasciculi proprii are clearing perceptibly, leaving the outline of the dorsal spino-cerebellar tract

FIG. 5.—Sixth thoracic segment.

quite distinct, but still in such numbers as to obscure the ventral tract's border. The largest portion of the dorsal spino-cerebellar tract lies ventrally.

Thoracic VI (fig. 5).—The dorsal spino-cerebellar tract is still, though less distinctly, in two parts due to it capping the now slightly curved pyramidal tract. Its shape here resembles that of an inverted dipper, the "bowl" lying against the posterior horn, the "handle" against the lateral border of the cord.

Ventrally this "handle" is distinctly separated from the ventral spino-cerebellar tract, and the spino-cerebellar bundles appear as separate entities. The ventral spino-cerebellar tract is a very thin bundle of fibres along the ventro-lateral edge of the lateral column. A few fibres at its dorsal extremity are arranged in a small circle.

Cervical I (fig. 6).—There is little change, except that the great bulk of the

dorsal spino-cerebellar tract seems to be situated dorsally. The "handle" has become very thin and short, while the dorsal part is quite thick and compact. The break in the contiguity between the two tracts is greater and is filled with scattered fibres, the bulk of them being placed further medial from the edge of the cord. These will be designated in future as "intermediate fibres." The ventral spino-cerebellar tract, too, is moving somewhat dorsally and widening out, its thickest part being dorsal.

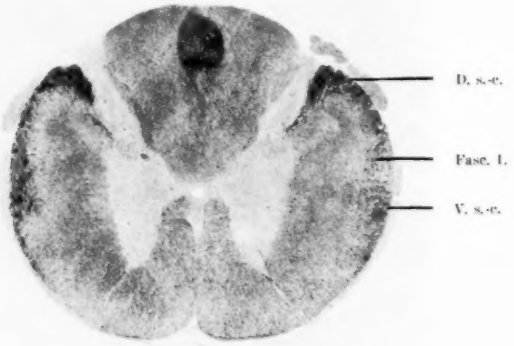


FIG. 6.—First cervical segment.

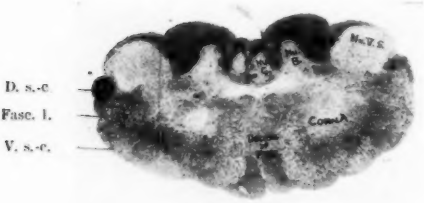


FIG. 7.—Level of decussation of the pyramids.

The level of the decussation of the pyramids (fig. 7).—The dorsal spino-cerebellar tract is a fairly concentrated, circular mass extending medialwards from the periphery of the cord, ventral to the nucleus of the spinal fifth root It is separated from this nucleus by the narrow band of the tractus spinalis trigemini. The intermediate fibres stand out rather prominently. The ventra spino-cerebellar tract is a more or less scattered bundle situated at the border of the cord.

At the lower level of the inferior olive (fig. 8) the nucleus of the lateral funiculus with its superior projection, the accessory nucleus, is very prominent. On the left the dorsal spino-cerebellar tract projects mesially from the border of the cord, its ventralmost extension lying between the ventral portion of the spinal fifth root and the accessory nucleus of the lateral funiculus. On the right side the dorsal spino-cerebellar tract is seen as an oval mass of fibres capping, as it were, the accessory nucleus of the lateral funiculus.

The ventral spino-cerebellar tract lies along the lateral border of the lateral nucleus at the extreme edge of the cord. It does seem here as if some few fibres of the ventral spino-cerebellar tract, or perhaps of the intermediate

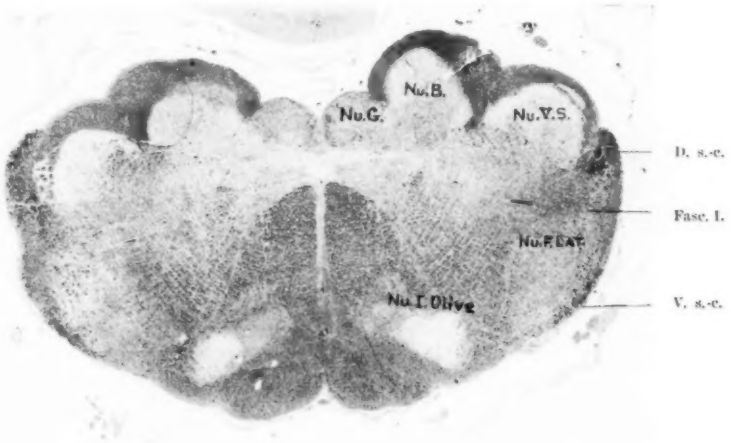


FIG. 8.—Level of caudal portion of inferior olive.

fibre group, go into the nucleus of the lateral funiculus but apparently do not terminate there.

The two portions of the nucleus of the lateral funiculus are continuous masses of grey matter. The ventral spino-cerebellar tract fibres lie ventral to it, while the dorsal spino-cerebellar tract is dorsal. The intermediate fibres are seemingly contiguous with the degenerated dorsal spino-cerebellar tract. They, too, lie dorsal to this irregular mass of grey matter in the lateral funiculus.

The lowest folia of the inferior vermis are present in this section; no degenerated fibres are found in these lobules. In the more cephalad portion of this block we find the dorsal spino-cerebellar tract creeping rapidly dorsalwards. It appears to come out laterally from below the spinal fifth root and curl around the dorso-lateral periphery of the hind-brain, opposite the nucleus of the restiform body.

Fig. 9.—The dorsal spino-cerebellar tract becomes elongated and thin

tapering at each end and extends between the dorsal surface of the nucleus of the spinal fifth and the middle of the nucleus of the restiform body. The ventral cerebellar tract has remained in the same relative position it occupied more caudally, but is here rather broadened. The cerebellar vermis contains fine granules of degeneration in the declive and the pyramis, and a very little in the uvula. This degeneration comes from the inferior contingent of fibres of the dorsal spino-cerebellar tract.

Fig. 10.—On the right side the dorsal spino-cerebellar tract has spread even

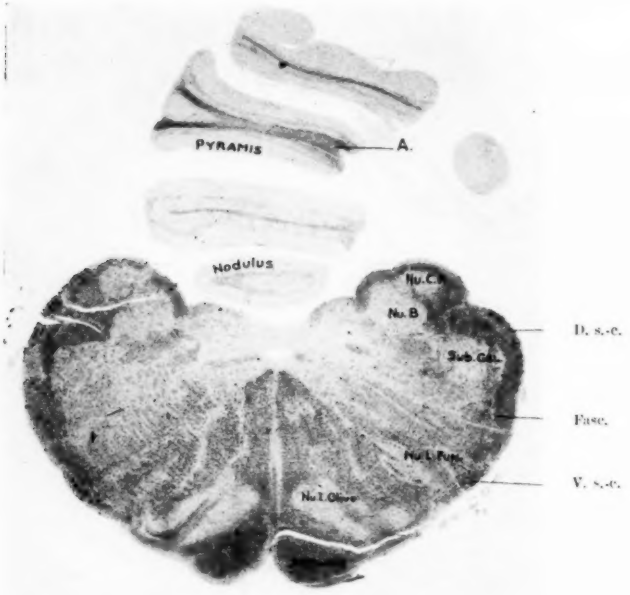


Fig. 9.—Level of nucleus of the restiform body.

further dorsalwards, curling around the nucleus of the restiform body, while on the left side (which is cut a little higher) this bundle of fibres is situated entirely dorsal. At its most mesial part it is beginning to "bunch" up in a whorl-like arrangement. The ventral spino-cerebellar tract remains in about the same relative position as in the more caudal sections.

There is considerable degeneration in the declive from the dorsal spino-cerebellar bundle; the fibres are offshoots from the inferior contingent of this tract which streams through the pyramis. The hemisphere is entirely free from degeneration.

Fig. 11.—On the right we find the dorsal spino-cerebellar tract "bunching"

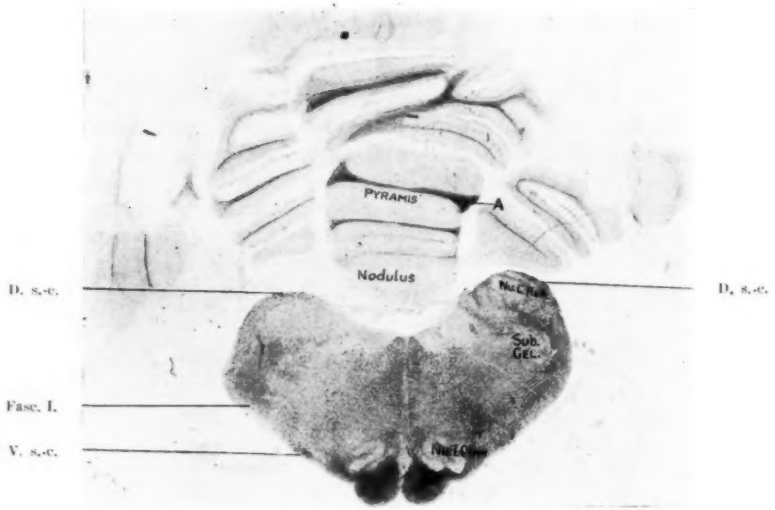


FIG. 10.—Level of the inferior portion of the cerebellar hemispheres.

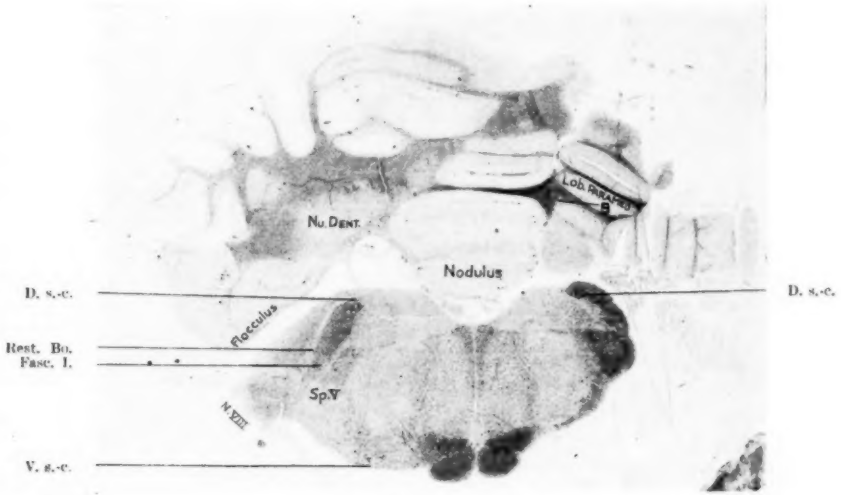


FIG. 11.—Level of nucleus dentatus.

up in the restiform body, whereas on the opposite side, where this body has already been firmly established, the round dorsal spino-cerebellar tract occupies its dorso-mesial aspect.

The ventral spino-cerebellar tract on the left is arranged in skeins among and along the fibres of the trapezoid body opposite the nucleus of the seventh nerve. It is to be observed that the ventral spino-cerebellar tract is here circumscribed; its fibres are associated with the lateral lemniscus only opposite the facial nucleus; some filaments seem to run towards this nucleus, but do not enter it. However, from the appearance of the ventral spino-cerebellar tract on the right side, which is just a little further caudal, one can see plainly

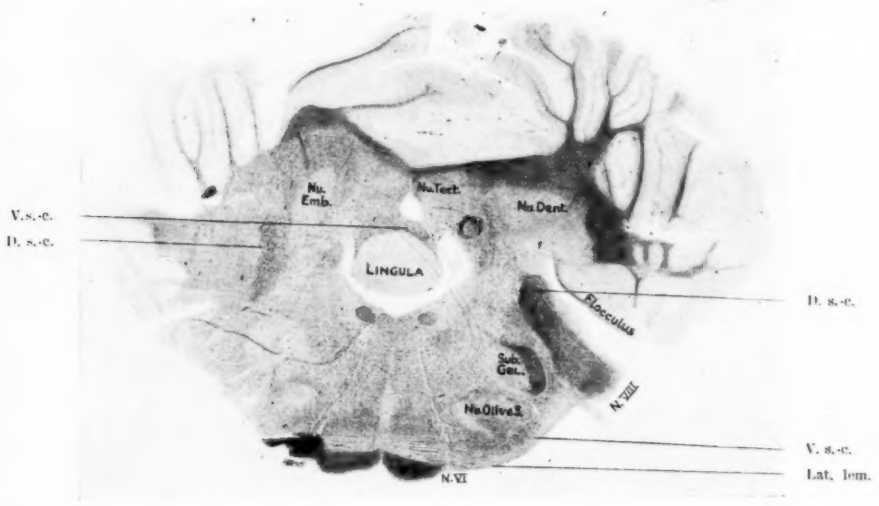


FIG. 12.—A section through the more caudal portion of the superior vermis.

that the ventral spino-cerebellar tract changes its relative position but little. On the left may be seen the central grey matter of the cerebellum and sparse degeneration granules in the stalk of the flocculus. The large grey mass extending to the ventral portion of the flocculus is no doubt the dentate nucleus. The triangular-shaped white matter (of pyramis) present on the right side of this section, through which the descending dorsal spino-cerebellar fibres stream, contains a few collaterals going into the paramedian lobule of the hemisphere.

A section through the more caudal portion of the superior vermis (fig. 12).—On the right the dorsal spino-cerebellar tract appears as a compact, round mass of heavily stained fibres in the mesial and dorsal parts of the inferior peduncle of the cerebellum. On the left side, however, it is climbing dorsally around the nucleus emboliformis.

In the space just dorsal to the lingula, in the exact middle of the vermis, a very few of the most caudal fanning fibres of the ventral spino-cerebellar tract are seen. They are fanning into the vermis after their very short backward course dorsal to the uncinate bundle of Russell. This spreading occurs caudal to the corresponding fibres of the dorsal tract. The ventrally placed, purely ascending portion of the ventral spino-cerebellar tract is here found in the meshes of the lateral lemniscus along the lateral border of the superior olive.

A section through the superior vermis (fig. 13).—The right ventral spino-cerebellar tract is spreading *en masse* into the vermis, the great bulk of its fibres going to the lobulus centralis, but many enter the culmen, and a

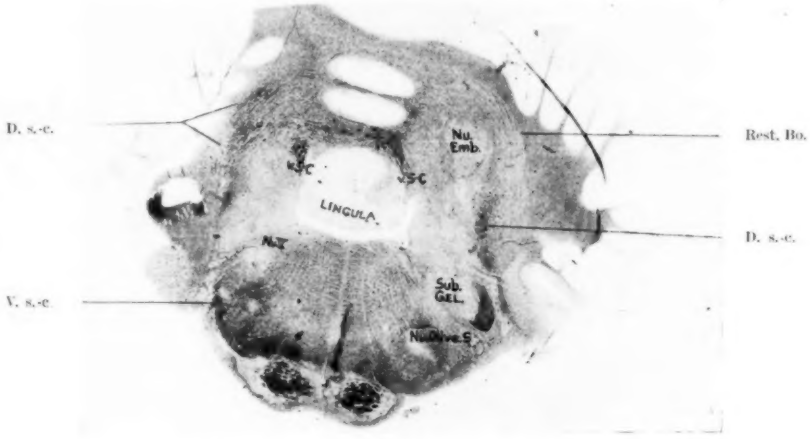


FIG. 13.—Section through the superior vermis.

large-sized contingent the lingula. On the right side the dorsal spino-cerebellar tract can be seen running dorsalwards alongside the nucleus emboliformis. The ventral portion of the ventral spino-cerebellar tract is still seen in the meshes of the lateral lemniscus fibres.

On the left side the dorsal spino-cerebellar tract is seen radiating into the vermis. The superior peduncle is already well formed and these fibres of the dorsal spino-cerebellar tract lie dorsal to it.

The ventrally placed part of the ventral spino-cerebellar tract on this side again becomes quite compact opposite the superior olive, just ventral to the outgoing fibres of the trigeminal nerve.

At the junction of the lingula with the white substance of the hemispheres, the portion of the ventral spino-cerebellar tract which turns backward into the vermis to terminate, is present as a compact bundle. This section, then,

demonstrates the ventral or ascending portion of the ventral spino-cerebellar tract, the short dorsal part which turns backward into the vermis, as well as its fanning termination. It will be seen that most, if not all, of the terminating fibres cross to the contralateral side in the anterior commissure of the cerebellum.

Fig. 14.—On the right side the great dorsal spread of the dorsal spino-cerebellar tract into the superior vermis is seen. This occurs considerably lateral to the mid-line; some few fibres can be observed to run across

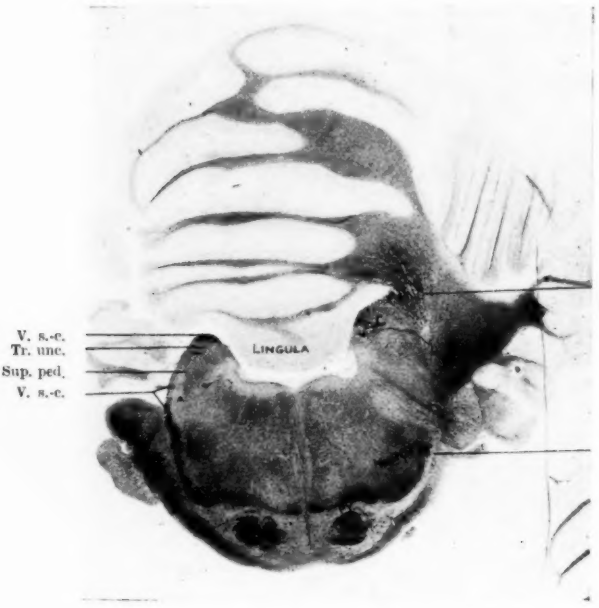


FIG. 14.—Section just above the fifth nucleus.

the uncinate bundle of Russell. Both the dorsal and ventral portions of the ventral spino-cerebellar tract are compact bundles. On the left, however, the ventral spino-cerebellar tract swings around the dorsal border of the anterior hind-brain, dorsal to the above-mentioned uncinate bundle.

Cat 16.—*Small black male. Killed twelve days after operation. Marchi-Busch stain. Paraffin embedding. Sagittal sections.*

March 18: Section of the right ventral and dorsal spino-cerebellar tracts in the first lumbar segment.

April 1: The animal was sacrificed. Brain and cord were removed and immersed in 10 per cent. formalin.

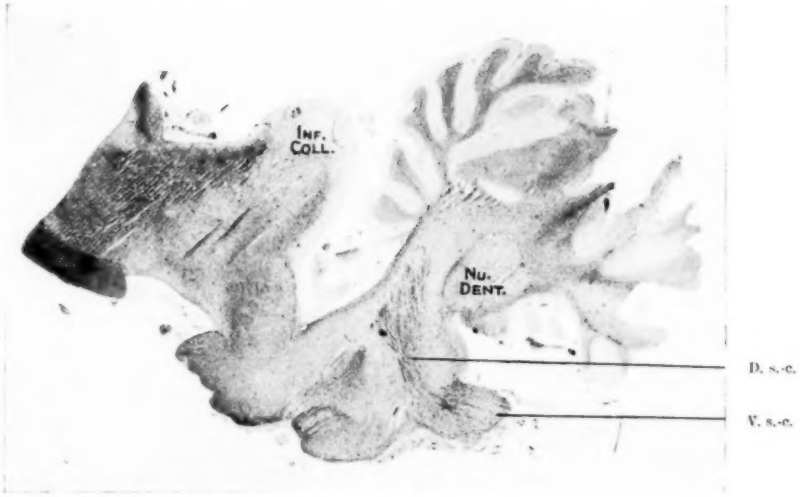


FIG. 15.—Extreme lateral sagittal section.

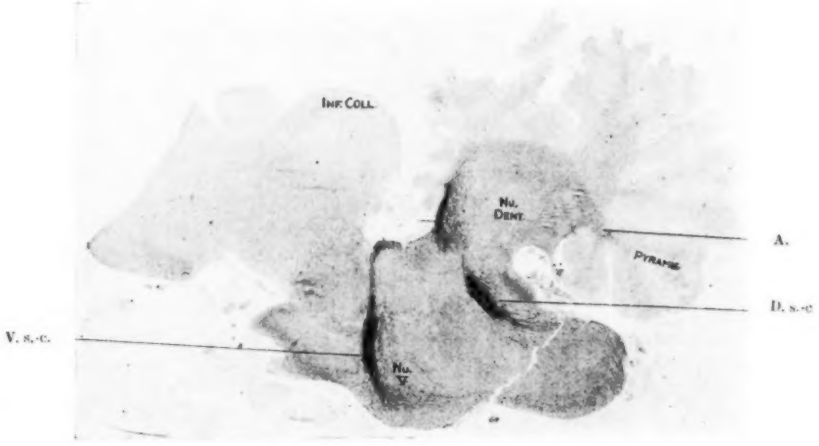


FIG. 16.—Lateral sagittal section.

April 15: The cord and brain were taken from formalin and cut into seventeen transverse cord blocks and eleven sagittal brain-stem sections 3 mm. in thickness. The latter were counted from the left to the right, i.e.. from the uninjured to the injured side.

From here the procedure was similar to that of the preceding experiment, excepting that this material was embedded in paraffin instead of celloidin. The sections of the cord were embedded with the lower surface placed anteriorly; the brain-stem blocks were arranged so as to bring the right side anteriorly.

It is unnecessary to describe the sections of the cord as they resemble very closely those already described, except in the scarcity of degeneration on the left side, the side opposite the lesion.

Only sections of the right half of the brain, that is of the side of the lesion, will be described. Both spino-cerebellar tracts on this side are considerably degenerated. The left, or contralateral side, has, on the other hand, a very sparsely degenerated dorsal spino-cerebellar tract and a slight, almost negligible degeneration in the ventral spino-cerebellar tract.

The extreme lateral portion of the right cerebellar hemisphere is not here considered because of the difficulty of orientation in such a small block. In the transverse sections of Cat 2 this area contained no degeneration.

Fig. 15.—The heavily stained fibres coursing up, above the most lateral grey mass of the cerebellum and curling over it, belong to the dorsal spino-cerebellar tract.

Fig. 16.—We see a distinct band of fibres, the ventral spino-cerebellar tract, curving round the fifth nerve in its journey dorsalward to obtain a position dorsal to the superior cerebellar peduncle. It is clear that the fibres travel through the brain-stem in the same plane that they assume after looping around the fifth nerve.

The dorsal spino-cerebellar tract is spreading into the cerebellum in a fountain-like arrangement. In man the dorsal spino-cerebellar tract and the other fibres of the restiform body swing dorsalwards in the cerebellar white matter lateral to all the cerebellar grey nuclei, closing them in, as it were. In the cat, the dorsal spino-cerebellar tract curves over a rather prominent mass of grey matter, so we have to assume that in this animal the dorsal spino-cerebellar tract does not pass external to the dentate, for if it did there would be a more laterally placed nuclear mass to be identified. The dorsal spino-cerebellar tract winds lateral to the nucleus emboliformis on its way through the white matter of the cerebellum.

Fig. 17.—The fanning fibres of the dorsal spino-cerebellar tract are beginning to terminate, whereas the ventral spino-cerebellar tract is a rod-shaped structure just dorsal to the uncinate bundle of Russell and definitely separated from the terminating fibres of the dorsal spino-cerebellar tract. A fairly heavy contingent of degenerated dorsal spino-cerebellar tract fibres go into the inferior vermis (pyramis mainly) just dorsal to the grey nuclei of the cerebellum. The ventral spino-cerebellar tract is still as heavy a bundle as it was more laterally, apparently not losing any fibres.

Fig. 18.—The majority of the few mesially placed terminating fibres of the dorsal spino-cerebellar tract end in the superior folia. A few of these fibres terminate in the inferior lobules of the vermis; in sagittal sections they

Fig. 17.—Sagittal section.

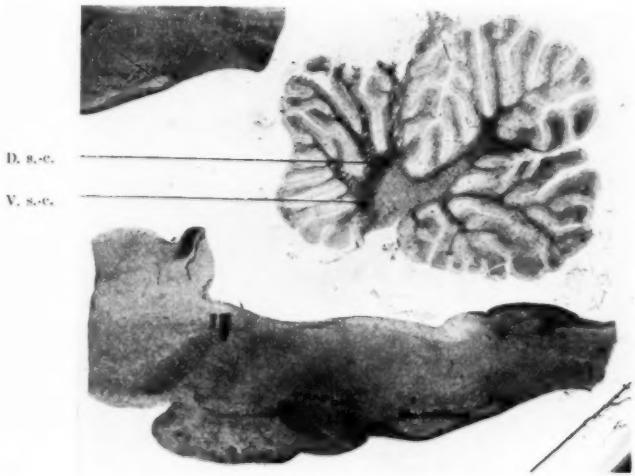


Fig. 18.—Mesial section.

cannot be seen connected with either of the spino-cerebellar tracts more cephalad, but it may be assumed from transverse sections that they are part of the few mesially terminating dorsal spino-cerebellar fibres.

comparative number of the crossed and uncrossed fibres with any degree of accuracy, but it does seem that the greater part do cross. This, it is believed, is substantiated by the appearance of the fanning fibres of the ventral spino-cerebellar tract in sections in the transverse plane.

Cat 11.—*Male, black. Survived operation for twelve days. Horizontal sections. Marchi-Busch stain. Paraffin embedding.*

March 5, 1926: Section of the two lateral tracts at the eighth thoracic segment on the right side.

March 20: Cat sacrificed: brain and cord removed and put into 10 per cent. formalin.

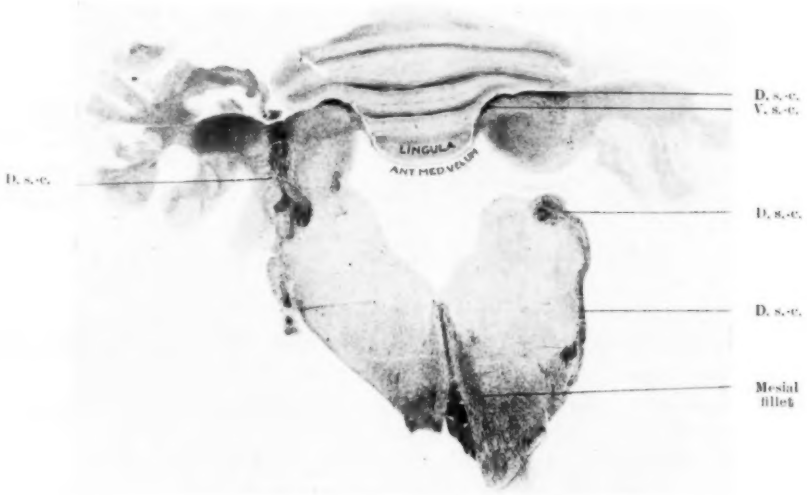


FIG. 20.—Horizontal section through restiform body.

April 3: Material removed, cut and immediately put into Marchi-Busch fluid. There were twenty-two transverse blocks of the spinal cord, and eight horizontally cut brain-stem blocks. These tissues were treated as in the previous experiments. They were embedded in paraffin and sectioned at 40 μ. The blocks were embedded so that the inferior surface lay uppermost.

Fig. 20.—Above the nucleus of the lateral funiculus the dorsal spino-cerebellar tract is a compact bundle on the lateral border of the hind-brain. It makes two distinct curves lateralwards in ascending to enter the inferior peduncle of the cerebellum. On the right it is a circular mass in the forming restiform body, just lateral to the vestibular nuclei. From here, as may be seen on the contralateral side, the fibres in the restiform body, having first

The oval band of fibres lying just below the lobulus centralis is the ventral spino-cerebellar tract; it is almost as compact and as large as it was more laterally. This again demonstrates conclusively that very few fibres have left this ventral spino-cerebellar contingent to seek their end stations laterally. This section is, roughly, about the most mesial plane in which purely dorsal spino-cerebellar tract fibres terminate. No doubt mesial to this plane some few fibres of this tract do end, but the number is small. The bulk of the terminal fibres in this region are from the ventral spino-cerebellar bundle.

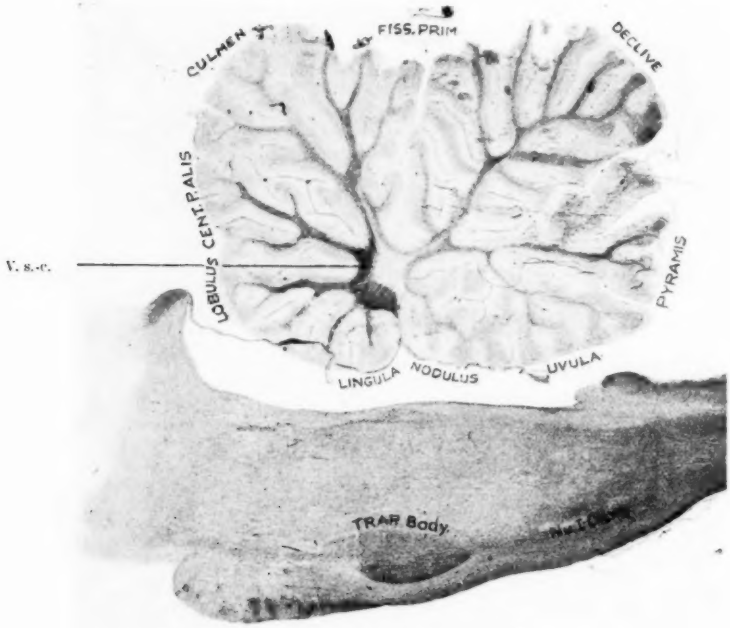


FIG. 19.—Extreme mesial section.

Fig. 19.—The ventral spino-cerebellar tract can be seen breaking up in the folia of the superior vermis, mainly in the lobulus centralis and the anterior portion of the culmen, but a fair-sized group of fibres goes to the lingula. No fibre of the ventral spino-cerebellar tract can be followed into the inferior vermis. The fibres of this tract extend to the opposite side of the vermis, as far as the superior peduncle. Owing to the sparsity or almost absence of degenerated ventral spino-cerebellar fibres on the contralateral side in the cord and medulla, these fibres must cross through the great cerebellar commissure. It is impossible, from this type of section, to estimate the

(*A*) *Course and Termination of the Dorsal Spino-cerebellar Tract.*

It is interesting to note that this tract assumes various shapes in its ascent in the spinal cord and brain-stem. In the lowest lumbar regions it is a small oval bundle adjacent to the posterior root zone. The bundle then forms a thin crescent curving around and capping the crossed pyramidal tract; and a little more cephalad it has the shape of an inverted "dipper." The next gross change is at the level of the lateral nucleus of the medulla. Here it is shaped like the sector of a circle; the arc lies against the rim of the brain-stem, the apex extending between the spinal fifth nucleus and the nucleus of the lateral funiculus.

Higher it becomes much narrower as it rapidly climbs dorsalward, first lateral to the spinal fifth nucleus, then alongside of the nucleus of the restiform body. In the upper part of the posterior hind-brain the dorsal spino-cerebellar tract is extremely thin and fusiform, lying dorsal to the small remaining nucleus of Burdach and the nucleus of the restiform body. A most interesting change is that of a dorso-mesial whorl-like "bunching" in the restiform body, as that structure is being formed. Higher, where the inferior peduncle of the cerebellum is an anatomical entity, the dorsal spino-cerebellar tract has assumed a small, compact, circular form in its dorso-mesial part. It is to be observed that it occupies but a small part of the restiform body. This circular shape is retained until this bundle radiates into the cerebellar white matter, lateral to the nucleus emboliformis, to terminate in the vermis.

Of much interest, too, are the four distinct externally convex curves that the dorsal spino-cerebellar tract makes in its ascent into the folia of the vermis. The first three are in a horizontal plane, whereas the last is sagittal: (*a*) from the cord to the position between the spinal fifth root and the lateral nucleus of the medulla; (*b*) from this position to the restiform body; (*c*) in its ascent in the restiform body alongside the superior peduncle; and (*d*) finally, a portion of the terminal fibres, in their course into the inferior vermis. The latter curve in the sagittal plane as they arch around the intermediate grey mass of the cerebellum.

What are the end stations of the dorsal spino-cerebellar tract? It was shown in transverse and horizontal sections that the fanning out of this dorsal spino-cerebellar tract is much more lateral than that of Gowers' tract. It is true one cannot be certain that some few fibres of the more dorsal tract do not terminate in the mesial portion of the vermis with those of the ventral tract, but we know that the great bulk of the fibres do terminate laterally, uncrossed.

arranged themselves in a circle, ascend in the inferior peduncle to reach the superior cerebellar vermis, describing a third curve outwardly.

These fibres then fan out loosely, sagittal to their plane of ascent in the brain-stem. Mesially and contiguous with the more loosely arranged dorsal spino-cerebellar tract in the cerebellar white matter, lies the heavy and compact ventral spino-cerebellar bundle. It has arrived dorsal to the uncinate bundle after a loop around the fifth nerve (shown so well in sagittal sections).

Fig. 21.—This is reproduced merely for the purpose of again bringing to the reader's attention that the ventral spino-cerebellar fibres terminate medially, while the great bulk of those ascending in the dorsal spino-cerebellar bundle terminate laterally.

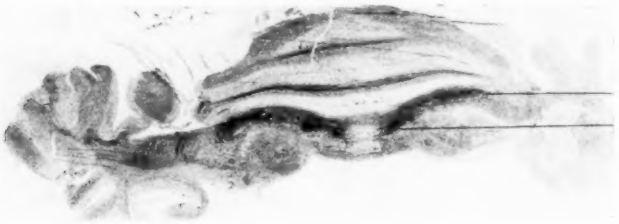


FIG. 21.—Horizontal section.

V.—DISCUSSION OF OBSERVATIONS.

Typical spino-cerebellar tract degeneration has been studied in sections in the three planes. It is now necessary to consider the material as a whole, correlating the appearances seen in one plane with those of the other two.

My observations are not really conclusive on the regional distribution of these two tracts, except, perhaps, as regards the lower levels from which the dorsal spino-cerebellar bundle is derived. This tract extends in the cat as low as the Lumbar V, and it would seem that it is present in fairly heavy concentration as low as Sacral I, and perhaps even in Sacral II. In the spinal cord sections in which a degenerated lateral cortico-spinal tract is visible below the lesion there is a clear, unmistakably outlined oval zone between the posterior horn and the degenerated crossed pyramidal tract. Above the lesion the degenerated dorsal spino-cerebellar tract appears in this very area. Further caudalward than Sacral I, this clear zone cannot be traced definitely, but it may extend down to Sacral II.

My investigation throws no light on the cells of origin of either spino-cerebellar tract.

Therefore, it becomes an important issue to think in terms of the sagittal planes of the folia of the vermis in considering the termination of both the dorsal and ventral spino-cerebellar tracts. The ventral tract is really much more circumscribed in its area of termination than the dorsal spino-cerebellar tract, as it ends only medially, approximately between the two superior cerebellar peduncles.

The group of degenerated fibres that can be seen sweeping into the inferior vermis passes through the triangular-shaped white substance of the pyramis. Just caudal to the grey nuclei of the cerebellum a very small number of these fibres send branches to a lobe of the hemisphere. According to the atlas of Winkler this lobule is designated as the paramedian lobe. This very small group of fibres is the only contingent of spino-cerebellar fibres that enters the hemisphere.

Fibres can be traced to the dorsal and ventral portions of lobulus centralis in large numbers, many go to the dorsal portion of the culmen and the dorsal part of the declive, and a goodly contingent sweeps into the pyramis. A few go to the uvula, tuber, and ventral part of the culmen. A very few degenerated fibres were observed in the stalk of the flocculus, but their exact course could not be determined. Their origin from the dorsal spino-cerebellar tract seems most likely.

We can then say that the dorsal spino-cerebellar tract terminates in the superior, middle and inferior vermis, while a very small group of fibres enters the hemispheres, and perhaps an even smaller number the stalk of the flocculus.

(*B*) *The Course and Termination of the Ventral Spino-cerebellar Tract.*

In the ascent of this ventral tract in the brain-stem, a relatively constant position is maintained, in comparison to its fellow, the dorsal spino-cerebellar tract. There is, however, a marked difference in the degree of concentration of its fibres at varying levels.

The first definite appearance of this bundle in the spinal cord is in the second lumbar segment (Cat 12). It is a thin arc of fibres here, lying along the ventrolateral border of the spinal cord. This relative position is retained throughout its upward course. At the level of the pyramidal decussation, perhaps slightly lower, the tract becomes a compact oval bundle. It retains this shape for a short distance, but on the gradual appearance of the nucleus of the lateral funiculus, the ventral spino-cerebellar tract is flattened by it and assumes a position around its ventrolateral border.

It again becomes concentrated into an oval bundle opposite the extreme dorsolateral surface of the inferior olive. There is but slight deviation of this tract lateralwards before the level of the superior olive is reached. At the level of the trapezoid body and the lateral lemniscus, strands of ventral spino-cerebellar fibres separate and spread among the ridges or grooves made by the fibres of the lemniscus, the largest bundle being towards the lateral border of the brain-stem.

Due perhaps to the fact that the superior olive projects slightly lateralwards, the ventral spino-cerebellar tract also follows this course. It thus makes a very slight outward curve. It constantly lies just lateral to this structure. As the highest level of this superior olivary nucleus is reached, the ventral tract once more becomes compact and somewhat triangular; it extends upwards in this way for a very short distance, then makes the loop around the fifth nerve, and takes a direct course dorsalwards.

Each fibre, after turning the loop, runs dorsad in a rather wide band in the same plane in which it starts. The band runs vertically until it has traversed the greater portion of its course, and then bends a little lateralwards. The fibres then spread along the dorsal aspect of the superior cerebellar peduncle, separated from it by the rather wide uncinate bundle of Russell.

The ventral spino-cerebellar tract advances in this way to become wedged in between the superior peduncle and the white matter of the lingula. It here is somewhat oval in shape, quite thin and very compact. In this position the ventral spino-cerebellar tract runs backward for a short distance, and fans out in the vermis just caudal to the corresponding fibres of the dorsal tract. These fibres terminate in and near the middle of the vermis.

In transverse sections it seems that many, if not the greatest number, of the fibres of the ventral spino-cerebellar tract cross to the other side in the great anterior commissure of the cerebellum. No fibre of the ventral tract either enters the inferior vermis or ends in any of the lobules of the hemispheres.

The ventral spino-cerebellar fasciculus is therefore distributed to the opposite and perhaps to the same side of the superior vermis, the bulk of the fibres going into the lobulus centralis, the dorsal part of the culmen, and a fairly large group into the lingula. No terminal fibres are found in the central grey masses or in the hemispheres.

There is no doubt that the question will be raised as to my conclusion that Gowers' tract terminates medially and Flechsig's laterally,

since both bundles were degenerated in all the experiments, but the two tracts appear as separate entities until near their ultimate terminations, and there is always either a difference in staining or in the compactness of the fibres. This is evident in the photographs.

There can be no doubt, in transverse as well as horizontal sections, of the more mesial fanning out of the ventral spino-cerebellar tract. The sagittal limits of the termination of the dorsal tract are not so circumscribed as those of its ventral fellow, but the great bulk of its fibres can be shown to terminate external to those of the ventral spino-cerebellar tract.

The position of the terminal fibres was first determined on examining transverse sections and observing the apparent small space in the vermis that the ventral spino-cerebellar tract occupies while radiating out. On examining brains cut in the sagittal plane the fibres of the dorsal spino-cerebellar tract were found in more lateral sections. Terminal fibres were seen coursing up and down from the compact dorsal spino-cerebellar tract in the white matter of the cerebellum, and as these were given off the compact dorsal spino-cerebellar tract diminished materially in size. A large part of that which remained could be observed to break up in the superior vermis.

In these sections the ventral spino-cerebellar tract is a compact fusiform group of fibres dorsal to the uncinate bundle. Further mesialwards this mass gradually moves into the white matter, but it is always demarcated from the terminating dorsal spino-cerebellar tract. It is only quite medial, after the bulk of the dorsal spino-cerebellar tract has broken up in the superior vermis, that the ventral spino-cerebellar tract starts to send off terminal fibres. It is impossible to determine exactly the point where the dorsal spino-cerebellar tract ceases and the ventral spino-cerebellar tract begins to send off fibres. There is no doubt an overlapping where the most laterally situated terminal twigs of the ventral spino-cerebellar tract appear.

The ventral spino-cerebellar tract terminates on the same as well as on the opposite side. The number of crossed fibres seems to be greater than those remaining on the same side. In no section could any fibre be traced from either tract to a central nucleus of the cerebellum. There is no evidence of any of the so-called "collateral plexuses."

Both these tracts terminate in the cerebellum and in it only. The spino-thalamic tract is said to ascend with the ventral spino-cerebellar tract, and after this has entered the cerebellum to join the dorsal margin of the mesial lemniscus and terminate in the thalamus. I have never

obtained degeneration of these fibres. One probable reason is that in the cord this tract is situated mesial to the ventral spino-cerebellar bundle and escaped injury, since the edge of the knife was directed lateralwards.

In man the dorsal spino-cerebellar tract, or rather the restiform body, is placed alongside of the dentate; no nucleus is found lateral to it. In the cat a large diamond-shaped nuclear mass is present in the white matter, extending to the ventral part of the flocculus. Cephalad this mass ends as the superior vermis is approached; and then we find the restiform fibres spreading out dorsalwards and enclosing, as it were, not this extreme lateral grey mass, but the nucleus emboliformis which lies mesial to it. Either in the cat we have an unaccounted for grey mass, which is most unlikely, or the inferior peduncle swings around the intermediate cell mass. The latter view is held by the author.

It was particularly interesting to find what a comparatively small area of the restiform body is occupied by the dorsal spino-cerebellar fibres. This little round group of tightly arranged fibres is huddled into its dorso-medial part. There is but little doubt but the bulk of the peduncle is made up of olivo-cerebellar fibres in the cat.

The constant occurrence of the loose intermediate fibres is a surprising feature. They are a rather loosely arranged group of degenerated fibres of large calibre, which lie between the ventral spino-cerebellar and the dorsal spino-cerebellar tracts. These fibres appear in the gap between the distinct spino-cerebellar tracts in the higher thoracic and cervical segments. At the level of the appearance of the nucleus of the lateral funiculus they turn medialwards, perhaps passing through it. The question must be considered whether these fibres belong to the dorsal or to the ventral spino-cerebellar tract, or are a separate bundle.

Pellizi, in 1892, may have had these fibres in mind when he described a median cerebellar tract. "To Gowers' and Flechsig's bundles a median cerebellar tract must be added, equally constant although smaller. It lies between the dorsal and ventral spino-cerebellar tracts in the cord and medulla. It is composed of large fibres. At the emergence of the seventh nerve its fibres tend dorsally, then dorsally turn inwards, and lie along the inner border of the ventral extremity of the ascending root of the spinal fifth. It thus comes into contiguity with the ventral tract, but the fibres of the two are always distinct one from another. The fibres are abundant in the caudal half of the middle peduncle and always lie in the internal part

of its radiations. They go towards the superior part of the superior vermis."

We find this group of fibres placed in the small space between the ventral and dorsal spino-cerebellar tracts all the way up the cord and brain-stem. This space between the two tracts increases as the spinal cord is ascended, and the irregularly placed but distinct group of fibres spreads out, always appearing in transverse section as if it were a loosely arranged connection between the dorsal and ventral tracts. In the first cervical segment these fibres tend to move medialwards, deviating a considerable extent from the periphery of the cord. As the lateral nucleus appears it seems to displace this tract even more mesialwards, so that it lies adjacent to the more ventral fibres of the dorsal spino-cerebellar tract, separated by this nucleus from the ventral spino-cerebellar tract, which here is ventral to the lateral nucleus.

When the inferior olive becomes a well-marked structure this small, loose fasciculus again recedes to the periphery, and once again we find the three tracts contiguous along the lateral border of the medulla. The intermediate tract here becomes looser, for it fills a larger gap than previously. As the brain-stem is ascended this bundle's most intimate association appears to be with the dorsal tract; there gradually develops a larger space between ventral spino-cerebellar tract and this intermediate bundle. While the restiform body is in formation this is quite definite. Where the cochlear branch of the eighth nerve winds around it all these loose fibres are included within the restiform body. At the dorsal part of the inferior peduncle the dorsal spino-cerebellar tract is found as a small black circle, and contiguous with its ventral border these loose, rather irregularly placed fibres lie, extending to its inferior point. There is a distinct zone between this area and the degenerated fibres of the ventral spino-cerebellar tract lying in the meshes of the lateral lemniscus.

As the dorsal spino-cerebellar tract makes its sweep dorsalwards to radiate into the lateral portions of the vermis, these fibres are lost to view as a distinct entity; they apparently sweep up with the degenerated fibres of the dorsal spino-cerebellar tract to end in the cerebellar vermis. We do not find them internal to the ventral part of the spinal fifth as Pellizi described; on the contrary they hug the lateral border of the brain-stem, except where they deviate mesially at the level of the lateral nucleus of the reticulum and in the restiform body.

If these fibres are part of the known spino-cerebellar tracts they are most closely associated with the dorsal spino-cerebellar tract. This is

especially obvious when the lateral nucleus appears, and after the triangular restiform body is established. But if they are part of the dorsal tract they are certainly of different nature from the rest of this bundle, which is distinguished by its compactness, while these intermediate fibres are loose and irregularly placed. It would then seem as if this small group of fibres is a spino-cerebellar fasciculus separate from the two well-known bundles. It might be designated "fasciculus spino-cerebellaris intermedius."

VI.—Two Problems evolving from the Investigation.

(1) Do these tracts cross in the cord? It cannot be said from my investigations that these tracts are either direct, or partially or totally crossed. The operative wounds did not injure their cells of origin but the tracts.

In many of the earlier papers where actual photographs are inserted, contralateral degenerations are shown, though but one side of the spinal cord was injured. Horrax [18] refers to the constant appearance of bilateral degeneration of the spino-cerebellar tracts after operations on one side and explained it by the assumption that the tracts cross.

I also found that in the greater number of my experiments both sides were about equally degenerated. It seemed extraordinary if only the most lateral tracts were divided that crossing fibres, if there are any, should be injured while the cells of origin were intact.

In a few spinal cords (figs. 22 and 23), with either single or double section of the spino-cerebellar tracts, the contralateral dorsal spino-cerebellar tract was represented by an almost negligible number of degenerated fibres; where there were perhaps about 400 degenerated fibres on the side of operation, eight or ten fibres only were degenerated on the contralateral side. These fibres were not arranged along the lateral border of this tract, but seemed to be homogeneously intermingled with the normal fibres. In other sections no contralateral degenerated fibres were found in the ventral spino-cerebellar tract, while on the operated side the tract was heavily stained. These observations show conclusively that the presence of bilateral degeneration of a spino-cerebellar tract after injury to one side of the cord is not due to a crossing of these tracts. In none of my sections was I able to find any fibre crossing to either of the opposite spino-cerebellar bundles, and many of my animals were kept alive over three weeks. Twenty-one days, according to Lewandowsky, should produce well-established secondary degeneration.

The spino-cerebellar tracts are situated at the border of the spinal cord, and it is not difficult to assume an injury of the contralateral side against the bony canal during the surgical operation; slight bruising may be sufficient to cause degeneration of the spino-cerebellar fibres.

FIG. 22.—Second cervical segment (Cat 3).

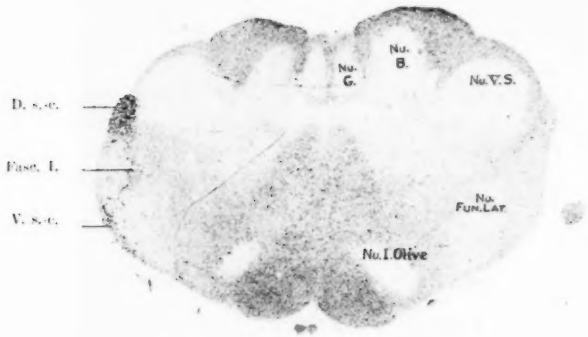


FIG. 23.—Level of caudal portion of inferior olive (Cat 3).

It has been advanced by Mott that this condition is due to disturbance of the blood-supply of the opposite side. This may be a factor, for, when but a few contralateral dorsal spino-cerebellar fibres were degenerated, they were distributed uniformly over the area of the tract, but it cannot explain the degenerations I have observed.

(2) Why do the dorsal spino-cerebellar and the ventral spino-cerebellar tracts alter relatively little in appearance, as they ascend the spinal cord from the site of injury?

After a lesion of the lower part of one posterior column, the uninjured fibres originating above the lesion are laid down alongside of the degenerated fibres, between them and the posterior horns. In a high segment the degenerated fibres from the lumbar-sacral segments occupy a small space near the mid-line, and appear compressed by the addition of normal fibres alongside them. This is very well demonstrated in the sections of the spinal cord of Cat 2.

We might expect a similar stratification in the spino-cerebellar tracts. Where are the normal fibres from higher segments placed if there is an injury of the inferior portion of this tract?

Sherrington and Laslett in 1903 stated that the tract is stratified in the following order: The outermost fibres come from the lowest sections of the cord; next, fibres from the lower thoracic segments, and deep to these fibres from the higher thoracic segments and the lower cervical segments.

In my sections it is easy to demarcate the dorsal spino-cerebellar tract from the crossed cortico-spinal bundle, because of the difference in the type of fibre. The motor tract is more compact and deeply stained than the tractus spino-cerebellaris dorsalis. It should be therefore easy to detect any crowding in of successive normal fibres, as we have two distinct borders the limits of which we can closely watch, i.e., the outer border of the cord and the junction of the dorsal fasciculus with the pyramidal tract. I have not been able to find any displacement in the sections of Cat 1, in which the cord was sectioned at the first lumbar segment. It is scarcely possible that all the dorsal spino-cerebellar fibres arise below the first lumbar segment, though the undegenerated bundle is of a fairly large size below this segment; in fact, there is but little appreciable difference between it and the degenerated tract above the lesion.

If Sherrington and Laslett found this stratification, may we not assume that after a lesion in the first lumbar segment (Cat 3) there ought to be in the cervical cord a large number of normal fibres added to those degenerated? But it would seem that the very little displacement of the degenerated fibres that has occurred is due only to the larger bulk of the pyramidal tract at this level.

VII.—Comparison of my Results with those of some Predecessors.

I believe, as do a number of preceding investigators, that none of the ventral spino-cerebellar tract fibres enter the inferior vermis. Schäfer and MacNalty and Horsley traced a small number of its fibres to this portion of the vermis, while Lewandowsky stated that practically all the ventral spino-cerebellar tract ends here—a few, perhaps, terminating in the nucleus funiculi lateralis. Ingvar, whose work is the most recent, did not trace any of the ventral spino-cerebellar tracts behind the fissura prima. With this I agree. Horsley's statement, in 1909, is an indication of the confusion regarding the termination of these two cerebellar tracts. "We cannot leave this most important question without drawing attention to various facts bearing on it which have curiously received support, so that even in the last edition of Quain's 'Anatomy' the statement is unfortunately made: 'The fibres from Gowers' bundle are distributed mainly to the inferior vermis.'" The works of MacNalty and Horsley and Ingvar are the two most complete on the topographical distribution of the fibres ending in the folia of the vermis.

Horsley and S. MacNalty demonstrated fibres of the ventral spino-cerebellar tract terminating in lobulus centralis, culmen and declive, while the dorsal spino-cerebellar tract entered the lobulus centralis, pyramis and declive. Ingvar, on the other hand, in investigation on cats, found that the ventral spino-cerebellar tract did not terminate below the superior vermis, but entered the lobulus centralis and culmen, while the dorsal tract ended in the lobulus centralis, culmen, declive, uvula and pyramis.

Horsley traced no fibres into the lingula, whereas, according to Ingvar, an almost negligible number terminates there. I found a very good-sized group from both the dorsal and the ventral spino-cerebellar tracts in this the most frontal folium of the superior vermis.

In the main I agree with Ingvar as to the folia of the vermis in which the dorsal spino-cerebellar tract terminates. My investigations show, however, a much larger group of fibres going into the lobulus centralis and declive, and a few entering the tuber. In agreement with MacNalty and Horsley I believe that few fibres go into the uvula.

In previous investigations there has been no discussion on the sagittal planes in which the bulk of each of the bundles terminate; I believe it necessary to consider not only the exact folia in which they end, but also the position of the fibres in relation to the mid-line.

In agreement with Lewandowsky, and not with André-Thomas, I found fibres entering, but not terminating in, the nucleus funiculus lateralis.

I cannot agree that there is a definite difference in the calibre of the two tracts under consideration, as advanced by Collier and Buzzard. It is true that usually there is a decided difference in their appearance. There are two reasons for this: firstly, there is a decided variation in the compactness of the two tracts, the ventral spino-cerebellar tract is in its greatest extent very loosely arranged in comparison with the ex-

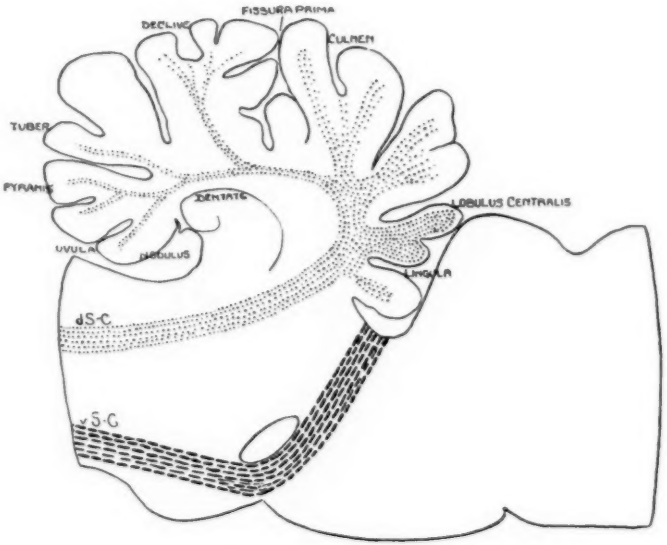


FIG. 24.—Lateral section.

tremely compact dorsal spino-cerebellar tract; secondly, owing to the method of operation, Flechsig's tract was as a rule much more injured than its ventral companion, and contained many more degenerated fibres. These two conditions make the individual fibres seem of different sizes, those of the dorsal spino-cerebellar tract appearing of larger calibre. But in sections of Cat. 7, in which the ventral spino-cerebellar tract was much more injured at operation than the dorsal spino-cerebellar tract, the ventral spino-cerebellar fibres appear larger.

In studying my sections I too was impressed with the apparent larger size of dorsal spino-cerebellar fibres. But when only the ter-

minating fibres of these two groups were seen together it was quite impossible to determine by the difference in size alone which fibres belong to either tract.

Summary.

(1) Two purely diagrammatic sketches are included to show my conception of the end stations of the ventral and dorsal spino-cerebellar tracts.

The first diagram is drawn to represent a lateral section of the brain-stem; the second a section near the mesial plane.

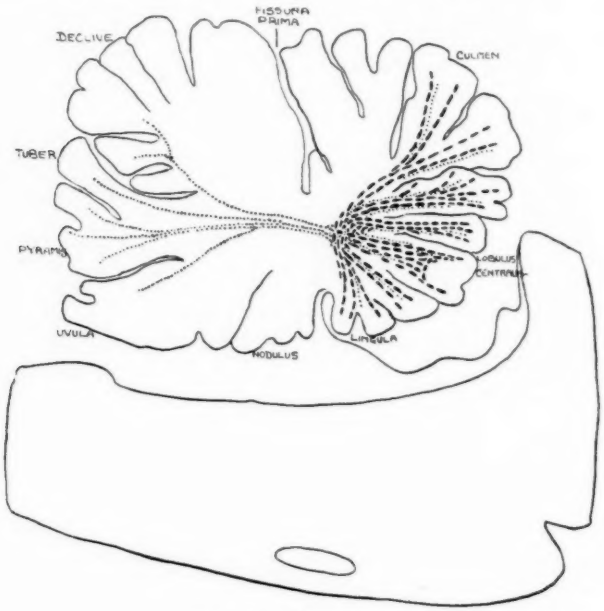


Fig. 25.—Medial section.

Flechsig's terminates laterally

(1) Lobulus centralis +++++ *
(2) Culmen (dorsal portion) +++
(ventral portion) +
(3) Declive (dorsal portion) +++
(4) Tuber +
(5) Pyramis +++
(6) Uvula +−
(7) Paramedian lobule of the hemispheres + −
(8) Lingula ++

Gowers' terminates medially

(1) Lobulus centralis +++++
(2) Culmen (dorsal portion) +++
(3) Lingula ++

* + indicates a small group of terminating fibres, ++ indicate a somewhat larger group, +++ a large group, and +++++ a very great number of terminal fibres. + and −, indicate but a sparse number of end fibres.

(2) The dorsal spino-cerebellar tract terminates in the vermis of the same side; the ventral spino-cerebellar tract goes mainly, if not entirely, to the vermis of the opposite side.

(3) The ventral spino-cerebellar tract fans out into the cerebellar vermis at a lower level than the dorsal spino-cerebellar tract.

(4) The dorsal spino-cerebellar tract extends as a large-sized bundle at least as low as the fifth lumbar segment.

(5) There is present a constant small group of fibres situated between the dorsal and ventral spino-cerebellar tracts, which is more closely related to the dorsal tract. We have designated it the "fasciculus spino-cerebellaris intermedius."

(6) The presence of degenerated dorsal and ventral spino-cerebellar tracts on the homolateral as well as the contralateral side, after a lesion of the spino-cerebellar tracts of but one side, is due to an injury of the contralateral side against the bony canal, and perhaps in a small measure to a disturbance of the blood-supply.

(7) There is no appreciable difference in the calibre of the fibres of the spino-cerebellar tracts

I should like to express my thanks to Professor Adolf Meyer, under whose guidance this work was performed; to Dr. C. Bagley, Jr., for assistance in the surgical part of the investigation, and to Miss Cecilia Bisson for the photomicrographs.

EXPLANATION OF ABBREVIATIONS ON FIGURES.

A. Inferior contingent of dorsal spino-cerebellar tract.
Ant. med. velum. Velum medullare anticum.
B. Fibres terminating in lobulus paramedianus.
Corn. a. Cornu anterius.
D. s.-c. Tractus spino-cerebellaris dorsalis.
Decuss. of Pyr. Decussatio pyramidum.
Fasc. i. Fasciculus intermedius.
Fasc. py. lat. Fasciculus pyramidalis lateralis.
Fasc. py. vent. Fasciculus pyramidalis ventralis.
Fiss. prim. Fissura primaria.
Inf. coll. Colliculus inferior.
Lat. lem. Lemniscus lateralis.
Lob. para. med. Lobulus paramedianus.
Nu. B. Nucleus of Burdach.
Nu. c. r. Nucleus corporis restiformis.
Nu. dent. Nucleus dentatus.
Nu. emb. Nucleus emboliformis.
Nu. f. lat. Nucleus funiculus lateralis.
Nu. G. Nucleus of Goll.
Nu. i. olive. Nucleus olivaris inferior.

Nu. olive. s. Nucleus olivaris superior.
Nu. P. O. M. Nucleus parolivaris superior.
Nu. tect. Nucleus tecti.
Nu. v. s. Nucleus spinalis trigemini.
Nu. v. Nucleus trigemini.
Py. Pyramis.
Rest. bo. Corpus restiforme.
Sp. v. Tractus spinalis trigeminalis.
Sub. gel. Substantia gelatinosa.
Sup. coll. Colliculus superior.
Sup. ped. Pedunculus superior.
Tr. unc. Tractus uncinatus of Russell. (Hook bundle.)
Trap. body. Corpus trapezoides.
V. s.-c. Tractus spino-cerebellaris ventralis.

LITERATURE.

[1] ACERBACH. (1) "Zur Anatomie der Vorderseitenstrangreste," *Arch. f. Path. u. Physiol. v. Virchow*, 1890, **121**, 199.
(2) "Zur Anatomie der aufsteigend degenerierenden Systeme des Rückenmarks," *Anat. Anz.*, 1890, **5**, 214.
[2] BASTIAN. *Med. Chir. Transactions*, 1867, **50**, 499.
[3] BECTEREW, V. W. "Die Leitungsbahnen im Gehirn und Rückenmark," Deutsch von Weinberg, Leipzig, 1898, II. Aufl.
[4] BERDEZ. "Recherches expérimentales sur le trajet des fibres centripètes dans la moelle épinière," *Rev. méd de la Suisse Rom.*, 1892, **12**, 300.
[4A] BING. "Die Bedeutung der spino-zerebellaren Systeme," Wiesbaden, 1907.
[5] BOUCHARD, CHARLES. "Des dégénérations secondaires de la moelle épinière," *Arch. gén. méd.*, 1861, **1**, 272, 441, 561, 578.
[6] BRUCE, ALEXANDER. "Note on the Upper Terminations of the Direct Cerebellar and Ascending Antero-lateral Tracts," *Brain*, 1898, **21**, 374.
[7] BRUCE, A. NINIAN. "The Tract of Gowers," *Quart. Journ. Exper. Phys.*, 1910, **3**, 391.
[8] COLLIER and BUZZARD. "The Degenerations resulting from Posterior Nerve Roots and from Transverse Lesions of the Spinal Cord in Man: A Study of Twenty Cases," *Brain*, 1903, **26**, 559.
[9] EDINGER. (1) "Anatomy of the Central System in Man and in Vertebrates in General" (Hall), 1899.
(2) "Ueber die Einteilung des Zerebellums," *Anat. Anz.*, 1910, **35**, 319.
(3) "Ueber der Fortsetsetzung der hinteren Rückenmarkswurzeln zum Gehirn," *ibid.*, Jena, 1889, **4**, 121.
(4) "Einiges vom Verlauf des Gefühlstammen im Centralennervensystem," *Deutsch. med. Wochenschr.*, 1890, **16**, 421.
[10] FLECHSIG, PAUL. "Die Leitungsbahnen im Gehirn und Rückenmark des Menschen, auf Grund entwicklungsgeschichtlicher Untersuchungen dargestelt," Leipzig, 1876.
[11] FOUVILLE. "Traité complet de l'anatomie et de la physiologie du système nerveux cérébro-spinal," Paris, 1844, p. 285.
[12] FRAENKEL, BR. "Die Kleinhirnbahnen der Taube," *Bull. de l'Acad. des Sciences de Cracovie*, 1909, **2**, 123.
[13] FREIDLÄNDER, A. "Untersuchen über das Rückenmarks und das Kleinhirn der Vögel," *Neurol. Centralbl.*, 1898, **17**, 381, 397.
[14] GEHUCHTEN, A. VAN. (1) "Le système nerveux de l'homme," Troisième Edition, Louvain, 1900.
(2) "Les voies ascendantes du cordon lateral de la moelle épinière," *Le Névraxe*, 1901, **3**, 159.
[15] GOWERS, SIR W. "Diagnosis of Diseases of the Spinal Cord," London, 1880.

[16] GRÜNBAUM, A. S. F. *Journ. of Physiol.*, 1894, **16**, 368.

[17] HOCHE, A. "Ueber sekundäre Degeneration, spezielle des Gowers'schen Bundels," *Arch. f. Psychiatr.*, 1896, **28**, 510.

[18] HORRAX, GILBERT. "A Study of the Afferent Fibres of the Body Wall and of the Hind Legs to the Cerebellum of the Dog, by the Method of Degeneration," *Anatomical Record*, 1915, **9**,1307.

[19] INGVAR, SVEN. "Zur Phylo- und Ontogenese des Kleinhirns,' *Folia Neuro-Biologica*, 1918, **11**, 105.

[20] KAPPERS, A., and FORTUYN. "Vergleichende Anatomie des Nervensystems," Haarlem, 1921, Bd. II.

[21] KUHN und TRENDELENBURG. "Die exogenen und endogenen Bahnen des Rückenmarks der Taube," *Arch. f. Anat. u. Physiol.*, 1911, Anat. Abteil., 35.

[22] KOHNSTAMM, O. "Ueber die gekreutz aufsteigende Spinalbahn und ihre Beziehung zum Gower'schen Strang," *Neurolog. Zentralbl.*, 1900, **19**, 242.

[23] LEWANDOWSKY, M. "Untersuchugen über die Leitungsbahnen des Truncus cerebri und ihren Zusammenhang mit denen der Medulla spinalis und des Cortex Cerebri," *Denkschriften der medicinisch-Naturwissenschaftlichen Gesellschaft zu Jena*, 1904, **10**, 98.

[24] LÖWENTHAL, N. "Dégénérations sécondaires ascendante dans le bulbe rachidien, dans le pont et dans l'étage supérieur de l'isthme," *Rev. méd. de la Suisse Rom.*, 1885, **5**, 511.

[25] LUBOUSCHINE, A. "La dégénérescence ascendante et descendante des fibres de la moelle épinière," *Le Névraxe*, 1901, **3**, 123.

[26] MCNALTY, S., and HORSLEY, V. "On the Cervical Spino-bulbar and Spino-cerebellar Tracts, and on the Question of Topographical Representation in the Cerebellum," *Brain*, 1909, **32**, 237.

[27] MARBURG, OTTO. "Zur Frage des Anterolateraltraktes von Gowers," *Monatsschr. f. Psych. u. Neurol.*, 1903, **13**, 486.

[28] MAY, W. PAGE. "The Afferent Path," *Brain*, 1906, **29**, 742.

[29] v. MONAKOW, C. "Experimenteller Beitrag zur Kenntniss des Corpus restiforme, des ausseren Akustikuskernes und deren Beziehungen zum Rückenmarke," *Arch. f. Psych.*, 1883, **14**, 1.

[30] MOTT, FREDERICK. (1) "Ascending Degenerations resulting from Lesions of the Spinal Cord," *Brain*, 1892, **15**, 215.

(2) "Experimental Enquiry upon the Afferent Tracts of the Central Nervous System of the Monkey," *ibid.*, 1895, **18**, 1.

[31] OBERSTEINER, H. "Anleitung beim Studium des Baues der nervösen Zentralorgane," Leipzig and Vienna, 1914.

[32] PATRICK, HUGH. "On the Course and Destination of Gowers' Tract," *Journ. Nerv. and Ment. Diseases*, 1896, **23**, 35.

[33] PELLIZI, G. B. "Sur les dégénérescences secondaires dans le système nerveux central, à la suite des lésions ou de la section des racines spinalis," *Arch. Ital. de Biol.*, 1895. **24**, 89.

[34] QUENZEL, F. "Ein Fall von Sarkoma der Dura spinalis: Beitrag zur Kenntniss der sekundären Degenerationen nach Rückenmarkskompression," *Neurolog. Zentralbl.*, 1898, **17**, 482.

[35] ROTHMANN, M. (1) "Ueber die sekundären Degenerationen nach Ausschaltung des Sacral und Lendenmarksgrau durch Rückenmarksembolie beim Hunde," *Arch. f. Anat. u. Physiol.*, 1899, Physiol. Abth., 120.

(2) "Die sakrolumbale Kleinhirn-seitenstrangbahn. Ausscheltung der grauen Substanz des Sakrolumbarmarkes durch Anaemie beim Hunde," *Neurolog. Zentralbl.*, 1900, **19**, 66.

36] ROSSOLIMO. "Ueber den centralen Verlauf des Gowers'chen Bundels," *ibid.*, 1898, **17**, 935.

[37] RUSSELL, R. "Contributions to the Study of Some of the Afferent and Efferent Tracts of the Spinal Cord," *Brain*, 1898, **21**, 145.

[38] SCHÄFER, E. A. "Some Results of Partial Transverse Section of the Spinal Cord," *Journ. of Physiol.*, 1899, **24**, 22, 32.

[39] SCHÄFER and BRUCE. "The Cerebellar Tracts of the Spinal Cord," *ibid.*, 1906-7, **35**, 49.

[40] SHIMAZONO, J. "Das Kleinhirn der Vogel," *Arch. f. Mikroskop. Anat.*, 1912, **80**, 397.

[41] v. SOLDER, F. "Degenerierte Bahnen im Hirnstamm bei Lesion des unteren Cervicalmarkes," *Neurolog. Zentralbl.*, 1897, **16**, 308.

[42] SHERRINGTON, C., and LASLETTE. "Remarks on the Dorsal Spino-cerebellar Tract," *Journ. of Physiol.*, 1903. **29**, 188.

[43] v. SINGER, J. "Ueber die Veränderungen am Rückenmark nach zeitweilen Verschliessung der Bauchaorta," *Akad. der Wissenschaften zu Wien*, 1887, **3**, 95.

[44] TESTUT. "Traité d'anatomie humaine," Paris, 1893.

[45] TOOTH, HOWARD H. "On the Destination of the Antero-lateral Ascending Tract," *Brain*, 1892, **15**, 397.

[46] THIELE, F., and HORSLEY, V. "A Study of the Degenerations observed in the Central Nervous System in a Case of Fracture-dislocation of the Spine," *ibid.*, 1901, **24**, 509.

[47] THOMAS, ANDRÉ. (1) "Le cervelet: étude anatomique, clinique et physiologique," Paris, 1897.
(2) "Cerebellar Functions" (Herring), 1912.

[48] TSCHERMAK. "Ueber den centralen Verlauf der aufsteigenden Hintenstrangbahnen und deren Beziehungen zu den Bahnen im Vorderseitenstrang," *Arch. f. Anat. u. Physiol.*, 1898, Anat. Abth., 291.

[49] TÜRCK, L. "Ueber sekundäre Erkrankung einzelner Rückenmarksstränge und ihren Fortsetzungen zum Gehirne," *Zeistchr. d. k.k. Gesellsch. u. Aerzte zu Wein*, 1852, **8**, 511; 1853, **9**, 289.

[50] UGOLOTTI, F. "Sopra un caso di lesione traversa completa del midollo lombare, Contributo allo studio delle degenerazioni ascendenti," *Annali di Nevroglia*, 1906, **24**, 10.

Proceedings of the Section of Neurology of the Royal Society of Medicine.

The Significance of Mirror-writing. (Abstract.)

By MACDONALD CRITCHLEY.

MIRROR-WRITING may be defined as writing which runs in an opposite direction to the normal, each individual letter being reversed; the script is therefore illegible until held up before a looking-glass. Since the original description by Leutilius, in 1688, mirror-writing has been described a great many times in the most diverse cases and in all manner of individuals. It must be realized that the faculty of mirror-writing can be acquired by anyone after a little practice. In the following table the various circumstances are set out, favourable for the appearance of mirror-writing.

THE ÆTIOLOGY OF MIRROR-WRITING.

(1) *Spontaneous.*

(*a*) Certain cases of right hemiplegia (with left hand).

(*b*) Certain normal children who are learning to write (either hand).

- (1) Complete mirror writing.
- (2) Fragmentary reversals.

(*c*) Some backward children and feeble-minded adults, particularly when associated with left-handedness (usually with the left hand).

(*d*) Cases of congenital word blindness (either hand). (The reversals are usually partial only.)

(*e*) In the left-handed script of sinistrals who have been taught to write with their right hand (under special circumstances).

(*f*) Cases of Little's disease (left hand).

(2) *Experimental.*

(*a*) Bi-manual writing .. .. } In normal subjects.
(*b*) Forehead writing (either hand) .. .. } In normal subjects.
(*c*) Writing on the under surface of a board (either hand) .. } In normal subjects.

(*d*) During states of inattention or partial obfuscation of consciousness (with either hand).

- (1) After blows on the head.
- (2) During hypnosis or in hysterical trance states.
- (3) Intoxication with alcohol, ether, or *Cannabis indica*.
- (4) During mental abstraction.

In the case of post-hemiplegic mirror-writing, some degree of aphasia and apraxia are also present as a rule. It is probable that the writing employed by Leonardo da Vinci in his famous note-books was the result of an apoplectic stroke.

The early efforts at writing by normal children are frequently characterized by reversals of isolated letters or words; amongst the insane, mirror-writing is not uncommon, particularly in their left-handed efforts.

Amongst the experimental circumstances under which mirror-writing is seen, simultaneous bimanual writing—dextrad fashion with the right hand and

sinistrad or mirror-fashion with the left—is very common. Mirror-writing is sometimes seen in cases of partial switching off of consciousness or attention, as during recovery from concussion or after depressant poisons. It may be obtained under hypnosis or in the trance states of hysteria. Finally, it may be seen in states of mental abstraction; thus Mills and also Fuller have seen telegraphists jotting down messages with their left hand mirror-fashion, whilst their right hand was held on the key.

The theories that have been hazarded to explain mirror-writing are very numerous; briefly they are of two main types: the physiological and the psychological. It appears, however, that no explanation is adequate to explain all the known facts which does not include both of these factors combined in different degrees in different cases.

Dealing first with the physiological aspect, it must be pointed out at the outset that abduction or centrifugal movements are the most natural for both hands; thus—if one goes to the blackboard with a piece of chalk one naturally draws a line from left to right when the chalk is held in the right hand. If the chalk is held in the left hand the line will instinctively be drawn from right to left. Similarly, a circle drawn with the right hand is executed in a clock-wise direction, if drawn with the left hand in an anti-clockwise direction. This is exemplified in the familiar actions of turning a screw or stirring a tea-cup. In other words the most natural movements of one hand are the mirrored replica of the other. When one attempts to write with the left hand the pen is moved in an adductive or centripetal direction and is found to be clumsy, difficult, and unnatural. In fact dextrad writing with the left hand actually conforms more to the nature of drawing. But if the pen is made to travel mirror-wise the movements are found to be easier and quicker, once the initial strangeness is overcome.

In spontaneous bimanual writing, a pen being held in each hand, one finds the left hand naturally executing mirror-writing. In fact it is almost impossible for the left hand to write otherwise, just as it is impossible for the left hand to draw one letter while the right hand is drawing a different one.

In other words the natural movements for the left hand are the reflections of those of the right hand. They are the most automatic and the least conscious.

On the face of it, therefore, one would expect writing performed with the left hand to be the mirrored opposite of that traced by the right, since such movements entail the innervation of identical neurones in the same order.

One believes that the repetition of such a highly complex act as writing facilitates subsequent performance of the same act, so that in time, writing becomes more and more automatic, and less and less a question of attention and volition. In the left motorium of right-handed individuals, therefore, there is gradually built up a complex of transcortical pathways which used to be referred to as the "writing centre."

In certain cases of damage to this left-sided motorium, the patient immediately adopts the style of writing mirror-fashion with the left hand: such a

performance may be completely foreign to the experience of the patient, who possibly has never before written with the left hand. How can one explain this sudden taking over by the right hemisphere of a function acquired by the left only after years of repeated trial and perseverance? Are we in a position to assume a potential writing centre co-existing in the right brain? Or is this phenomenon the result of the storing up in both hemispheres of kinesthetic memories, or memory of the muscle movements necessary to the act of writing? In this connection we are reminded vividly of Hughlings Jackson's conception of the duality of the brain; in his own words " . . . I hope to show two things: (1) That both halves are alike in so far that each contains processes for words; (2) that they are unlike, in that the left only is for use of words for speech, and that the right for "other processes in which words serve." Later he states . . . "the right half of the brain is for the automatic reproduction of movements of words, and the left side for their voluntary reproduction."

We may now say something about the psychological aspect of mirror-writing. We have affirmed that mirror-writing is actually the most natural mode of writing for the left hand. The question that must now be faced is why we do not all write in that way with our left hands.

The reason is largely one of education; we have learnt as a result of experience, that European languages arbitrarily read from left to right, consequently mirror-writing at once strikes us as being incorrect and probably illegible. The faculties of attention, perception and recognition are therefore ever-present agencies which check the inherent and more primitive "motor complex," which, if allowed its own way, impels the left hand to write from right to left.

Under circumstances in which these faculties of perception and recognition are in abeyance, left-hand mirror-writing is apt to appear. Thus in patients who have been poisoned with alcohol or ether, or who are recovering consciousness after concussion, these faculties are temporarily inhibited and in such circumstances mirror-writing may appear. In cases of severe damage to the left brain the same factors are present, favourable for the appearance of mirror-writing. The same set of circumstances obtains in feeblemindedness, and in hysteria.

In the case of children learning to write there persists for some little time an element of doubt as to the correct orientation in space, not only of letters but even of words, which, after all, is purely an arbitrary arrangement. This is particularly true in the case of children who attempt to write before they have completely mastered their letters. This indecision accounts for the occasional reversals of letters or words seen in the earliest efforts at penmanship in many normal children. Indeed, even in some uneducated adults the same doubt persists, so that one sees not uncommonly the letters S or N printed the wrong way round.

If normal children occasionally show such disorientation and confusion in writing, much worse are the mentally retarded children and those suffering

from congenital word blindness. Gordon has estimated the proportion of mirror writers to be over sixteen times more common amongst children in mentally defective institutions than in the ordinary preparatory schools. Of these defectives, mirror writers were more frequent amongst the left-handed scholars; to every one right-handed child there were fifteen sinistrals who wrote mirror-wise. This preponderance may depend in part upon the fact that the left hand is the one preferred for the finer and more co-ordinated movements. Accordingly, movements in that hand tend to be less voluntary and more automatic than those of the opposite side; here, again, are the same factors which predispose towards the appearance of mirror-writing.

We are forced to conclude, therefore, that a combination of circumstances, physiological and psychological, is necessary for the appearance of mirror-writing. The physiological factor, or "motor complex," gives us the innate predilection towards centrifugal movements with the left arm. This tendency, in the case of writing, is normally checked, however, by certain psychological factors, e.g., attention, perception and recognition, which may be spoken of as the "intellectual complex." When this latter is in temporary abeyance, the motor complex is apt to predominate and produce the phenomenon of mirror-writing.

In conclusion, a word or two about the development of the modern alphabet, which, although scarcely of neurological importance, does bear an interesting analogy with the subject of mirror-writing.

Our modern alphabet is derived from the Phœnician, a language which is essentially of Semitic character and reads from right to left. The early Græco-Roman races and the various Mediterranean tribes, borrowed the Phœnician alphabet, adapting it slightly. The point of interest lies in the fact that the earliest of these known inscriptions—in the Cretan and Etruscan dialects—were written in archaic Greek characters, and ran from right to left. This mode of writing then changed, but for a period of about two hundred years there was considerable doubt as to the orientation of letters and words. Consequently we find the early Greek and Latin inscriptions running alternately from right to left and left to right, the direction of each letter depending upon the direction of the words. Such a style of writing is referred to as the *βουστροφεδον* or ox turns, so called because it resembles the tracks made by an ox in ploughing a field. By about the third century B.C., the Greek and Latin languages were uniformly dextrad in direction.

The reason for this change is not at first clear, but the speculation made by Krahmer and Korst, if still unproved, is at least worthy of investigation. They published figures to show that the Semitic races whose writings read from right to left were predominantly left-handed people and probably wrote with the left hand. The Semitic peoples whose inscriptions read from left to right (such as the Assyrians and Babylonians) were certainly right-handed, as anyone can verify by examining the carvings of that period. The suggestion is that a change in direction of the handwriting coincided with and was due to an alteration in the handedness of the race; and that in modern races sinistrals predominate among those who write in a sinistrad direction.

Notices of Recent Publications.

Nervous and Mental Disorders from Birth through Adolescence. By B. Sachs and L. Hausman. Pp. 861. New York: Paul Hoeber. London: H. Milford. 1926. Price 50s.

Many nervous and mental diseases assume in children forms different from those which characterize them in the adult, and certain nervous affections are met with in the young only. The neurology of early life consequently deserves separate treatment. Several textbooks devoted to it are in existence, but the book under review is the most comprehensive treatise on the subject in the English language. It will prove useful as a work of reference, but its chief feature and most valuable asset is the incorporation in it of the wide personal experience of its senior author. It is essentially his own views that Sachs presents to his readers, though where necessary authorities are cited, and a short biography of the subject of each chapter is provided. The clinical sections are undoubtedly the most interesting, in fact the only criticism that can be advanced is that the descriptions of the morbid anatomy and pathology of some of the more important diseases are diffuse and incomplete. The essential nature and the pathogenesis of the various conditions included in Little's disease, for instance, deserve more discussion than they have received here.

The greater part of the book is occupied by the organic nervous diseases; this is followed by chapters on the functional and toxic diseases, endocrine disorders, vasomotor and trophoneurotic disorders, and finally, a section on mental affections. One of the most noteworthy chapters is on the "Normal Child, the Normal Youth, Development and Training," in which Sachs writes on the general management as well as on the training and education of the child and youth. Here he subjects to a pitiless analysis the grosser errors of psycho-analysis and points out the harm it may do to the child.

The chapters on the anatomy of the nervous system and on the methods of neurological examination, for which Hausman is mainly responsible, are admirable, though perhaps too detailed for a book of this character.

Thought and the Brain. By Henri Piéron. English Translation by C. K. Ogden. Pp. 262. London: Kegan Paul, Trench, Trübner and Co. 1927. Price 12s. 6d.

The original French edition of this interesting book has been already reviewed in this Journal (*Brain*, 1923, xlvi, 353). The English translation will, it is to be hoped, bring it to the notice of more students in this country, though no one had the excuse of difficulty in following the lucid French of the author. The translation has been on the whole well done, though in places a too rigid adhesion to the original has produced a rather stilted style and sometimes even inaccuracies.

Travaux et Mémoires. Par PIERRE MARIE. Tome 1. Pp. 358. Paris: Masson et Cie. 1926. Price 30 francs.

This is the first of a series of volumes in which Professor Pierre Marie intends to reprint some of his more important contributions to medicine. He has fortunately decided not to edit or alter in any way the original text, so that the reader will find here the incomparable descriptions he first gave to so many newly recognized conditions. The collection of these papers is particularly welcome, since many of them originally appeared in journals which are no longer procurable, or are to be found only in the larger libraries. The articles reprinted are not arranged in any definite order, either chronologically or by their subjects. Those in the first volume are "Aphasia," "Acromegaly," "Spondylose rhizomélique," "Pulmonary Hypertrophic Osteo-arthropathy," "Hereditary Cleidocranial Dysostosis," and "Achondroplasia in the Adult."

An Introduction to the Theory of Perception. By Sir J. H. PARSONS. Pp. 254. Cambridge: University Press. 1927. Price 18s.

The neurologist not less than the psychologist must be interested in such a complete presention of the subject of perception as is furnished in this volume; both the physiological significance and the psychological fate of afferent impulses are fully discussed, in fact many of its pages deal with impulses which in man at least reach no stage of consciousness. The whole treatment of the subject is admirable, and especially the attitude of the author that progress in psychology depends upon the security of the biological foundations on which it rests.

The main thesis developed is the universal existence, in higher mammals at least, of a dual mechanism, a more primitive *dyscritic* system on which an *epicritic* is superposed. This is largely based on Head's theory, the term protopathic being displaced by dyscritic, which in addition to its afferent features is distinguished by the fact that it excites "all-or-none" reactions and tends to initiate "mass reflexes." Although he does not accept Head's views in their entirety, he scarcely gives in their discussion due weight to many of the objections that have been brought against them, even where cutaneous sensation only is concerned, nor emphasizes sufficiently that Head has employed these terms in dealing with the peripheral nervous system only, and excluded them from his classification of sensory integration in the higher levels of the nervous system. Even when the author's own terms are accepted, the validity of his assumptions that sensibility can be divided into two systems, a dyscritic which is found in its most characteristic form in the lower vertebrates, and a new epicritic which appears in the higher animals, will probably fail to meet general acceptance. This dual mechanism is sought in smell, taste, hearing, and vision too, and the term dyscritic is even applied to varieties of motor response. Further investigations may confirm this hypothesis, but the reader can scarcely avoid the impression that the author shows an undue tendency to impose his

own ideas of order and simplicity on the work of nature. Even in the case of vision, the sense most elaborately discussed, this attempt to demonstrate a dual mechanism is far from convincing. The most interesting chapters are those in which the author discusses the reactions of the organism to afferent impressions, and backs up his views with a wealth of quotation and authority. The sections on instinct, perceptual patterns, induction, and those on the perception of space and of movement, are models of clear exposition, in which difficulties often overlooked are faced and discussed fully.

The extremely difficult task of giving a concise yet clear picture of the comparative anatomy of the brain, and of the evolution and significance of its different parts in different stages of its phylogenetic development, is essayed in fifty pages. This task is generally better reserved for the comparative anatomist who is familiar with the complexity of the subject and the risk of a too free interpretation of his observations, and the omission of this chapter would not have detracted from the value of the book, or even from the main thesis advanced in it. The direct deduction of function from structure is always dangerous, and some of the conclusions accepted in this section, and more especially some used later as arguments in favour of the theory of a dual mechanism of sensation, will not fail to excite controversy. It is, for instance, extremely doubtful if the posterior quadrigeminal and the median geniculate bodies are the main end-stations for such afferent impulses as can be called dyscritic, if the median geniculate bodies have mainly vestibular functions, or if such an anatomical differentiation of visual connections as is postulated corresponds with facts.

The volume as a whole can be, however, strongly recommended as a clear and stimulating introduction to a difficult but extremely important subject.

Anatomie topographique du Système nerveux central. Par G. GUILLAIN et I. BERTRAND. Pp. 322, avec 60 planches. Paris: Masson et Cie. 1926.

This is an atlas rather than a textbook on the anatomy of the central nervous system. It contains sixty plates, on many of which two or more drawings or photographs are reproduced. The text is written around these plates and is mainly descriptive of structures represented in the figures. The drawings are accurate and the photographs are well chosen and admirably reproduced. The descriptions are fairly full, and will enable the student who studies the anatomy of the brain in the anatomical laboratory to orientate himself easily in the sections before him, but the topographical method selected will not assist him to acquire readily a knowledge of the connections and relations of different structures, which is after all the essential part of nervous anatomy. The text seems to be on the whole accurate, but it is not to Brodmann that the credit belongs of having shown that the cerebral cortex varies in structure in different parts of the brain.

Paralysestudien bei Negern und Indianern. Von F. Plaut. S. 98. Berlin: J. Springer. 1926. Price 9·60 marks.

In 1925 the author and Kraepelin visited North America to investigate the frequency of and the type assumed by general paralysis among negroes and North American Indians. Their investigations were made in four mental hospitals, two in the United States, one in Mexico and one in Cuba. This volume, which records these observations, contains a large amount of information on the prevalence of syphilis in these races, the special forms it assumes, the frequency of general paralysis and its clinical features. The figures obtained indicate that in relation to syphilitic infection the North American negro is equally susceptible to general paralysis as the white races, and that on the whole it assumes the same clinical forms. Attention is drawn to the fact that the less complete treatment the negro generally receives in the early stages of syphilitic infection, than the white man, does not seem to increase the risk of general paralysis developing. Among the North American Indians general paralysis seems to be rare, but the race is certainly not immune. The disease is more common among the Mexican Indians, but many of the subjects are not of pure Indian blood. The views have been held that vaccination predisposes to general paralysis, and on the other hand that small-pox infection confers a certain amount of immunity. Plaut's observations do not support either of these hypotheses.

Shell-shock and its Aftermath. By N. Fenton. Pp. 173. London: Henry Kimpton. 1926. Price 12s. 6d.

The perpetuation of the term "shell-shock," as applied to war neurosis, is the chief adverse criticism that must be made in a review of this book; not only is it, as the author admits, inaccurate, but if the term continues to be used it will be a serious suggestive factor in later wars, and uneducated soldiers as well as the lay public will come to regard the conditions to which it is applied as inevitable, almost as honourable, consequences of exposure to gun-fire.

The author was during the war a neuropsychiatrist in an American Base Hospital in France, which received men with psychoneuroses who could not be returned to duty from the more forward medical units: they amounted to about 15 per cent. of the total. After his return to America he traced a large proportion of these cases in 1919-20 and again in 1924-25. The former census showed that 60·9 per cent. were engaged in full ordinary work, while five years later the percentage had risen to 80·8. During the same period the disabled group, who were unable to follow any remunerative occupation, had fallen from 21·7 per cent. to 9·4 per cent. This is the most interesting point brought out in the book.

Normale und pathologische Anatomie und Histologie des Grosshirns. By Professor Dr. A. JAKOB. Part 1. Pp. 457, with 270 illustrations, many of them in colour. Leipzig and Wien: Franz Deuticke. 1927. Price 60 M.

The subtitle of this book indicates that it is designed especially as a guide to the histopathology of the psychoses and the extra-pyramidal diseases. This, the first part, deals with the anatomy of the cerebral cortex and of the commissural paths passing to and from it, and with the general pathology of the brain. The first chapter is devoted to the development and comparative anatomy of the fore-brain, and the gross anatomy of the brain and its membranes and blood-vessels. The second section (100 pages long) commences with a description of the main commissural and projection systems from the cortex, but is chiefly devoted to a cytological study of the cortex. A more detailed survey of the development of the cortex is also given here, and we welcome especially the descriptions and illustrations of the cytology of the human cortex in the later stages of fœtal development, to which little attention is often given in textbooks of neuro-anatomy. The description of the various cortical areas follows the lines laid down by Brodmann and the Vogts, and is profusely illustrated, chiefly with photomicrographs. In the third chapter a short description is given of the nerve cell and fibre, the neuroglia and the blood-vessels. The microglia and oligo-dendroglia are well described and comparative pictures of the cortex and white matter, as seen by Nissl's stain and by Hortega's silver methods, are given. Unfortunately these come back to back instead of being face to face, so that comparison is difficult, but even so they are invaluable to the student.

The second part (260 pages long) deals with the pathological histology of the nerve cell and fibre, the neuroglia and the blood-vessels and meninges. This part is profusely illustrated with excellent coloured drawings and photomicrographs. The descriptions are full and richly documented, in fact, a historical résumé is given of the work on each subject from the days of Luschka to the very latest researches, even to some which still await publication. Much of the material bears the impress of the author's personal researches or of the closely followed work of his pupils, so that this part of the book has a very personal though by no means an egotistical character.

We look forward to the appearance of the second part of this excellent work.

Études sur les Affections de la Colonne vertébrale. Par ANDRÉ LÉRI. Pp. 526. Paris: Masson et Cie. 1926. Price .

This volume, which is profusely illustrated by photographs, radiographs and drawings, consists of a collection of papers now methodically arranged according to their subject matter, which Léri has written during the last twenty-five years. The importance of vertebral affections to the neurologist is evident, and will become more obviously so to anyone who reads through these

pages, for the observations recorded here reveal many conditions scarcely recognized in this country, and throw light on the pathology of other diseases with which we are more familiar. A short introduction is provided for each section, which in some cases merely indicates the points to be brought out, in others summarizes the salient features of the conditions to be described. The subject matter falls into four sections. In the first anomalies of development, as the various forms of spina bifida and the symptoms that may be associated with it, sacralization of the fifth lumbar vertebra and lumbalization of the first sacral, cervical ribs and errors in development of the first dorsal vertebra, are fully discussed. The second section deals with traumatic affections of the spine, and the third with spondylitis and vertebral ankylosis. The fourth section is devoted to vertebral rheumatism. The emphasis laid on treatment, and the detailed descriptions of operations and other procedures that may be necessary, are especially useful features of this volume.

Das Problem des Characteraufbaus. By Dr. HERMANN HOFFMANN, Privatdozent für Psychiatrie und Neurologie, Universität Tübingen. Berlin: Julius Springer. 1926. Price 12 M.

This volume is a careful analysis of the various views put forward, principally in Germany, regarding character types. The subject is becoming increasingly important, not only for pedagogy but for psychiatry, as a careful consideration of reaction type in its form and genealogy will prove of great diagnostic and prognostic value. The views of Jung and Weiniger are familiar to most of us and it is valuable to have brief and careful statistics of the views of Spranger, Klages and Müller-Reienfels. Kretchmer is considered in the light of his psycho-physical approach, and Ewart's character temperament formulæ are discussed. These are of value for pedagogy.

Kronfeld's classification takes due note of sociological backgrounds of type and hence his theories are of value to criminology. In this connection it is surprising that Birnbaum's treatment of criminal types is not considered (and criticized!). Historical characters and families are also dealt with, but naturally, in a book of this compass, all too briefly. Psychical compensations and effects upon type formation are considered and the Napoleon family receive very careful and detailed attention.

The later chapters on character abnormalities are full of value and references to well-known figures in the world of music abound.

Altogether it is a valuable compilation of the latest views on a new and profitable field of applied psychology.

Types of Mind and Body. By E. MILLER. Pp. 132. London: Kegan Paul, Trench, Trübner and Co. 1926. Price 2s. 6d.

Within the last few years several volumes have appeared on the classifications and relations of different physical and mental types, a subject which certainly merits further investigation. This small booklet, which is one of the

"Psyche Miniatures," is an excellent introduction to the matter by one who is familiar with its literature and yet maintains his own point of view. The manner in which the subject is treated cannot be better illustrated than a quotation from the introductory chapter: "We intend always to deal with tendencies; to trace the manner in which the dynamic processes within the organism tend to produce specific forms of bodily and mental reactions; to trace the physical and mental attributes that appear to crystallize out from such reactions; to show what the hinterland of character really is, and to mark off the frontiers that separate what are regarded as constitutional factors from what may be called conditional factors." The one regret the book raises is that the author has not chosen simpler language in which to present his views.

The Significance of the Physical Constitution in Mental Disease. By F. I. WERTHEIMER, and CLARENCE E. HESKETH. Medicine Monographs, No. X. Pp. 76. Baltimore, U.S.A.: Williams and Wilkins Co. Price $2.50.

This volume appears to be the only piece of research on the question of the relationship between physique and mental disorder which has appeared outside Germany. Stimulated by Kretschmer's "Körperbau und Character," it attempts and succeeds in verifying this author's correlation of the asthenic physique with the schizoid reaction type; and the pyknic physique with the cycloid reaction types. The authors of this monograph have gone into their physical determinants in a thoroughly scientific manner, that is, their first endeavour was to obtain a good anthropometric index. After working with the indices of Pignet and others, they devised one of their own, which would contain no numerical incommensurables, that is, all their figures are linear and volume determinations, for example, trunk and thorax capacities are taken as length and circumference.

It is of interest that Kretschmer's correlation has been again confirmed outside Germany, as his figures were mainly of Swabian origin, and therefore anthropologically limited. Figures of other national and racial groups should be collected to complete the correlation. The volume is interestingly illustrated with drawings of dominant physiques, and with tables comparing the various historical type distinctions. The bibliography is adequate.

Die psychopathischen Verbrecher. Für Aerzte und Juristen. Von Dr. KARL BIRNBAUM. Pp. 279. Second Edition. Leipzig: Geo. Thieme Verlag. 1926. Price 17.50 M.

The author of this considerable volume has already contributed much to German psychiatric literature relative to the psychoses and criminology. In this volume he brings together further matter to expound the earlier edition of 1914. The author tries to do full justice to the clinically separable classes, and marks off the severe physical conditions from those psychical deviations

which have had their origin either constitutionally or determined in early childhood, and which have remained stationary. He seems, however, to find some difficulty in relating the theoretically separated types—the medically pathological from the criminal, and to compromise he invokes a sociological standard to achieve the separation—a social-psychic function. This is not unlike the Ego-Ideal of recent Freudian psychology—which concept does something to bridge the gap between the personal and the social. The book is mainly concerned with a detailed consideration of the various types of character reactions—based mainly upon a faculty psychology—not a very dynamic conception, but for formal purposes not without its uses.

Simulation is considered in its psychopathological bearing, and a large chapter is devoted to forensic matters.

The volume is most suited to the forensic psychiatrist, and the division made by the author into clinical, pathological, and the socially criminal, should give relief to the psychiatrist and justification to the lawyer. This pragmatic solution is not unwise.

Psychotherapie. By Dr. MAX ISSERLIN, Professor an der Universität in München. Pp. 200. Berlin: Julius Springer. 1926.

After an historical survey of the subject the author divides his work into a general section and a special section. In the first half methods alone are considered, and a very large section is devoted to suggestion, with particular reference to hypnosis in practice and theory. This chapter is naturally followed by a discussion of ethical and re-educational approaches with which Du Bois has made us familiar. The dangerous affinities of these methods with suggestion is not stressed. The analytical methods are fully considered and criticized. Freud is approached on three critical points: firstly, the infantile sexuality theory; secondly, the mechanisms of displacement, conversion, psychical determinism; and lastly, the theory of analysis itself and the interpretation of its data.

The deviations from Freud expressed in the views of Jung and Stekel are considered.

The second half of the book deals fully with the symptomatic varieties of the neuroses and the application of psychotherapy to them. Disorders of childhood are dealt with from the same point of view.

One of the most striking deficiencies of the book is the absence of reference to Freudian theories of Ego development which have thrown some light on suggestion and the mechanism of the psychosis. These theories are at least worthy of criticism.

Die psychischen Heilmethoden. By various authors. Edited by Dr. KARL BIRNBAUM, Universität Berlin. Pp. 462. Leipzig: Geo. Thieme. 1927. Price 18.60 M.

In what is after all a small compass, the editor of this volume has collected together the best opinions in Germany on the various approaches to the study and practice of psychotherapy, and the ground is completely covered from

suggestion to the very latest dicta of Freud on Ego-psychology, and Kronfeld on psychotherapy in its educational aspect. The editor, in a lengthy introductory essay, deals with the psycho-physical problem and classifies organic and psychic neurosis. Dr. Ernst Solowicz discusses suggestion from Liebault to the Coué-Baudouin methods. The value of indirect suggestion is assessed as medicinal "Kuren" and physico-therapeutic approaches. Dr. Gustav Steyer deals minutely with various aspects of hypnosis and advances a reflex physiological theory. He enlarges upon its use in various conditions. Dr. Hattenberger devotes a considerable space to psycho-analytic and allied methods. Dr. Erwin Wrieberg writes of the asterian individual psychology and its application to the neuroses and to education. Dr. Kronfeld ends this volume with a consideration of psychotherapeutic education (or psychogogic!). This includes within its boundaries the value of work and ethical training for adults and children. The whole range of the "erotic motive" is analysed from various aspects.

With its series of bibliographies it is one of the most complete, if not the most complete, survey of the subject we have yet seen.

Die Grundlagen der Psychoanalyse. Von Dr. HEINZ HARTMANN. Pp. 192. Leipzig: Geo. Thieme Verlag. 1927. Price 9.60 M.

Psycho-analysis, as a method of approach in the study and cure of psychological disorders, must stand or fall by its ability to stand the test of scientific objectivity in the treatment of its data, and its fundamental concepts must be not merely working hypotheses, but also concepts belonging to the same orders of logic as do those of the other sciences. Few works on psycho-analysis proper attempt to examine the validity of the terms used, and fewer still are prepared to pass Ocklau's razor over the weedy overgrowths and redundancies. For this reason alone Dr. Hartmann's volume is welcome, in that it deals methodologically with this very vexing development in applied psychology. The book opens with a critical examination of psycho-analysis as a science, and as a branch of the mental sciences. He passes on to consider the validity of the free association method, and the unconscious, symbolism and the sex theories. A chapter is also devoted to the application of psycho-analysis to psychiatry.

On the whole, the theory scores definitely on the positive side, although the author warns us that, like the work of other psychologists, Freud's theories must inevitably suffer from the perspective of his own personality. A subject and author index is given.

Hygiène mentale. Par M. POTET. Pp. 599. Paris: E. Le François. 1926. Price 40 francs.

Professor Toulouse, in the preface of this book, defines the main object of mental hygiene as the preservation of the functions of the brain, and the establishment of rules of life which will allow each individual to make the best use of his powers with the least expenditure of nervous energy. Prophylaxis

and the early treatment of mental troubles are obviously important functions within its scope too, so that it touches intimately other branches, as social science, education, housing, employment and eugenics, as well as normal and morbid psychology and psychiatry. This wide field is surveyed by the author, in some places in considerable detail, in others the salient problems only being noticed. The sections on the principles of mental hygiene and their application to the individual as well as to a group of individuals, are an excellent indication of its sphere and of the results that may be expected when the new science is more fully developed. The succeeding chapters deal with the application of these principles to the early psychoses, abnormal children, criminality and the common intoxications, each of which would require a volume for its adequate presentation. One specially interesting feature of the book are the short reviews of what has already been done in other countries. Each section has its own bibliography and an index is provided.

Writers of "Original Articles and Clinical Cases" are supplied free of charge with 50 copies reprinted in the form in which the paper stands in the pages of 'Brain." If reprints are required in pamphlet form, with wrapper, title-page, &c., and re-numbered pages, they must be ordered, at the expense of the writers, from Messrs. BALE, SONS & DANIELSSON, Ltd., 83-91, Great Titchfield Street, London, W.

Members of the Neurological Section of the Royal Society of Medicine can obtain the Index of "Brain" for the Volumes I to XXIII inclusive, that is, from its commencement to the end of 1900, from Messrs. MACMILLAN & CO., Ltd., St. Martin's Street, London, W.C., at the price of 6s. 6d., post free.

To those who are not members of the Neurological Section of the Royal Society of Medicine the price is 8s. 6d. net, and the volume may be obtained through any bookseller.

EDITOR.